FEBRUARY, 1952

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Treatment of Intestinal Infections Associated with Low Grade Pathogenic Bacteria

A Roentgenographic Evaluation of the Common Measures Employed in the Treatment of Colonic Stasis

Nutritional Disturbances in Visceroptotic Patients

Gallbladder Disease

•

Seventeenth Annual Convention
New York, N. Y., 20, 21, 22 October 1952

VOLUME 19 NUMBER 2

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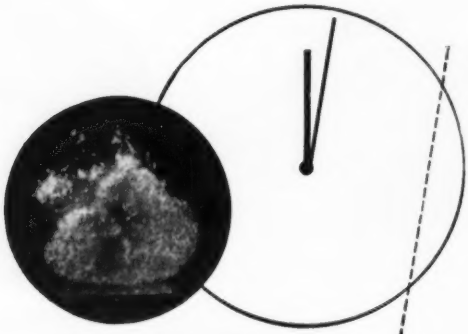

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

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SAMUEL WEISS, *Editor*

Business Office, 1819 Broadway, New York 23, N. Y.

DANIEL WEISS, *Managing Editor*

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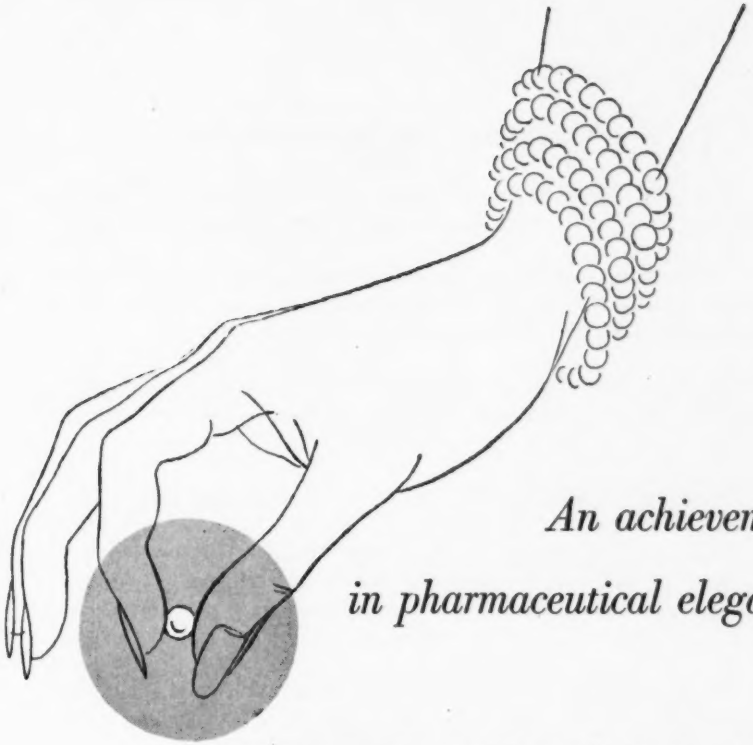

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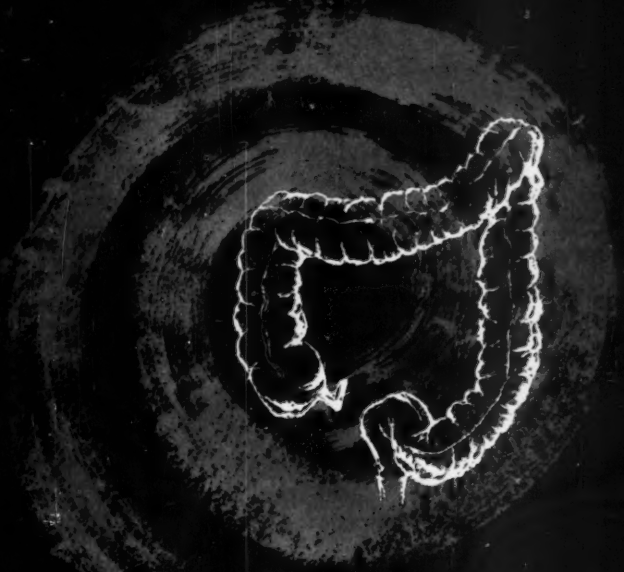

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NUTRITIONAL DISTURBANCES IN VISCEROPTOTIC PATIENTS*

GARFIELD G. DUNCAN, M.D.†

and

BARKLEY BEIDLEMAN, M.D.††

Philadelphia, Pa.

In this presentation we discuss a well known clinical combination—undernutrition and generalized visceroptosis. Many individuals are visceroptotic and yet enjoy apparently normal health. This fact has been used, and probably justly so, as an argument against considering visceroptosis as a disease entity. Visceroptosis is, nevertheless, an anatomical configuration which often increases markedly the difficulties in restoring to a normal state of nutrition those patients who have, because of dietary restriction or illness, lost appreciable amounts of weight, usually over a short period.

There is probably no more pathetic group of patients than those who are severely malnourished, have a marked degree of visceroptosis, and who, despite all efforts, have been unable to add to their weight, or to improve their health in general. The fatigue, lassitude, obstinate constipation, anorexia and malnutrition provide the background for the anxiety state which invariably develops. Almost without exception these patients give histories of having been subjected to exhaustive diagnostic studies and of having traveled from clinic to clinic, and it is usual that nothing strikingly relevant has been found, although this doesn't prevent the prevalent diagnosis of an "hormonal disturbance". The basal metabolic rate and excretion of corticoids are subnormal—a result of adaptation to the malnourished state and not to disease of the endocrine glands. It might be stated here that these patients are worse off when thyroid therapy is adopted, a result which might well be expected when the adaptive mechanisms are disturbed by increasing the metabolic rate at a time when it had become adjusted to the undernourished state.

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*Read before the Sixteenth Annual Convention of the National Gastroenterological Association, Chicago, Ill., 17, 18, 19 September 1951.

†Clinical Professor of Medicine, Jefferson Medical College, and Director, Medical Divisions of the Pennsylvania Hospital and the Benjamin Franklin Clinic.

††Assistant in Medicine, Jefferson Medical College; Assistant Physician to the Pennsylvania Hospital and Associate Physician to the Benjamin Franklin Clinic.

These sad patients are not exactly sick, neither are they well. Their chronic exhaustion, irritability and neuroses affect not only their own enjoyment of living but that of those about them—their physicians included. We can, without hesitation, say that formerly we dreaded seeing these patients. Their stories were long and the results of treatments were poor. Now the situation is different and the reason for this presentation is that these patients can be salvaged and restored to good health and the other benefits that ensue.

The clinical problems surrounding this large group of patients, predominantly of the female sex, comprise (a) the detection of the underlying disturbances and the appropriate appraisal of the influences which visceroptosis and undernutrition exert on the patients' well being, and (b) therapy and training of the patient.

TABLE I

Food Components	Recommended Daily Allowance	Percentage of Recommended Daily Allowance Ingested
Protein	60 gm.	51 to 83
Calories	2400	50
Calcium	1.0 gm.	80
Iron	12.0 gm.	82
Vitamin A	5000 I.U.	100
Ascorbic Acid	70.0 mg.	100
Thiamin	1.5 mg.	79
Riboflavin	1.5 mg.	96
Niacin	12.0 mg.	76

A survey of the pretreatment diet in the case of Mrs. H. S. (aged 53 years, height 5'1", weighing 77½ pounds and moderately active) illustrates the deficiencies in diet, notably in protein and calories, observed almost invariably in undernourished, visceroptotic patients.

DETECTION

Chief Complaints

Exhaustion
Underweight and an inability to gain in weight
Obstinate constipation
Nausea—on arising and after eating
Anorexia
Full feeling after a few mouthfuls of food.

HISTORY

Rapid loss of weight before onset of above complaints.

DIET SURVEY

Inadequate diet. The inadequacy of the dietary intake of these patients is depicted in Table I.

PHYSICAL EXAMINATION

Facies: Worried and wrinkled
Skin: Flaccid and inelastic
Weight: Considerably below normal
Muscles: Poor tone
Breasts: Atrophic
Liver and Right Kidney: Palpable
Abdomen: Lower portion protuberant and firm to palpation when the patient is erect, see Fig. 1.

Fig. 1—Patient M. M. illustrates the general physical appearance characteristic of undernutrition complicating a generalized visceroptosis without evidence of any other abnormality. Note the undernutrition, atrophic breasts, flaccid skin, protuberant abdomen and the fatigued appearance of the patient.

Roentgen Ray Studies:—A survey of the typical visceroptotic patient reveals the position of the stomach, small bowel, and colon, as illustrated in Fig. 2a, with the patient in the upright position. Studies of the urinary tract fre-

quently reveal kinking of the ureter as depicted in Fig. 3. It is remarkable how frequently ineffective nephropexies are done on these patients without apparent regard for the ptosis which reasserts itself when the patient assumes the upright position. It is customary to examine patients while they are recumbent and so the effect of a change in posture is easily overlooked by the casual examiner.

Further studies are unnecessary and, we believe, should not be done unless there are definite indications of other conditions that should be investigated. Too often the search for some obscure cause of symptoms in these cases gets one entangled in considerations of the minor deviations from normal, especially of endocrine and metabolic nature, which yield readily to correction of the abnormal nutritional state.

Rarely will the diagnosis be missed if every patient, who is undernourished and complains of exhaustion, is considered a subject of malnutrition complicating a visceroptosis until proven otherwise.

TABLE II

AN ILLUSTRATIVE FORMULA PROVIDING HIGH PROTEIN AND HIGH CALORIC VALUES IN 1100 C.C. OF LIQUID NOURISHMENT IS DEPICTED.

Diet Prescription		Ingredients	Household Measures
Protein	150 gm.	Lanolac Powder	2¾ cups
Fat	144 gm.	Water	3⅓ cups
Carbohydrate	400 gm.	Powdered egg	1 cup
Brewer's Yeast	30 gm.	Honey	1 cup
Volume	1000 c.c.	Cream	3⅓ cups
Total calories approximately	3500	Protenum	3 tablespoons
		Brewer's yeast	6 tablespoons
		Lemon crystals	2 tablespoons

The diagnosis of malnutrition in the visceroptotic patient having been made, it is usually a simple matter to restore the patient to normal health even though little change can be accomplished as far as the visceroptosis *per se* is concerned. The visceroptosis feature enters the picture merely because it renders it difficult, without special measures, for these patients to regain a normal body weight after having lost in weight as the result of one or more causes such as reduction by intent, a reduction due to diabetes, as illustrated in the case of D.R. (see Case 3), or to hyperthyroidism or following pregnancy or an acute illness.

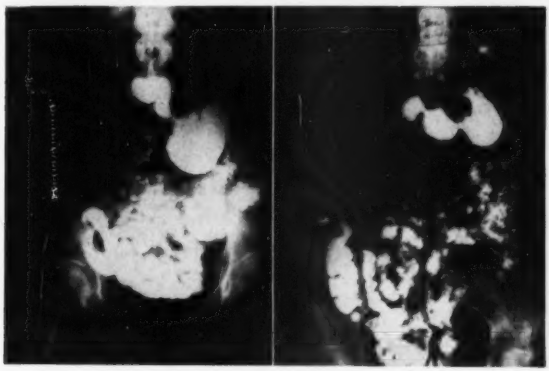
The ptosed stomach often empties poorly and small amounts of food give a sense of fullness and often one of nausea which tends to reduce the food intake to suboptimum levels. Anorexia is one of the most common symptoms of undernutrition and this vicious cycle is not broken until, by some means, an adequate nutritional intake is secured. It is when this is achieved that the patient usually

develops an excellent appetite for food. It is not generally appreciated, we believe, that undernutrition causes anorexia and usually it is not until an abundant intake is achieved that this symptom is replaced by a good appetite in the malnourished patient.

The treatment of these patients comprises:

1. Hospitalization—this we believe is essential. It breaks all connection with their current habits of eating and home problems. It permits opportunities to give reassurance—a most important feature—and of equal significance is the training of the patient in matters dealing with the diet. To embark on the treatment of these patients without the advantages which hospitalization offers is to court failure. We refuse to do it.

2. Diet. Ordinarily we prescribe a diet which provides approximately 150 grams of protein, with carbohydrate and fat sufficient to provide a total of 3,000



a b

Fig. 2—The degree of ptosis of the viscera, when the patient is in the upright position, as illustrated in *a*, is contrasted with the more nearly normal dispersion of the viscera when the patient is recumbent with the foot of the bed elevated, as in *b*.

to 3,500 calories. The high protein content is aimed at correcting the protein deficit which has arisen when body protein has been sacrificed for energy purposes during the long periods that the total caloric intake was insufficient.

The diet is served in 3 very small meals at a regular meal time and the balance, or more, is given in a liquid formula, a portion of which is given in the mid forenoon, one in the mid afternoon, and one at bed time. An illustrative formula is outlined in Table II.

Vitamin supplements are usually given also but are not considered essential. Patients who are unable to consume a complete nourishment are advised to lie down—with the foot of the bed elevated—for 20 minutes, after which time there

is rarely any difficulty in finishing the nourishment. That the position mentioned facilitates the emptying of the stomach is suggested by the fact that the stomach, though ptosed in the upright position, assumes a relatively normal position when the patient is lying down with the foot of the bed elevated (see Fig. 2b).

The physician's responsibility does not cease when he prescribed the diet. Failure is the rule unless his orders are followed through and it is seen to that the diet prescribed is actually ingested. In problem cases we have the dietitian weigh the leftovers and provide an accurate record of nourishments eaten. It is just as important to do this for these patients as it is to do it for diabetic patients.

3. The foot of the bed is raised 4, 6, or occasionally 8 inches. We believe that this measure aids in emptying the stomach after meals and also that it permits a more nearly normal dispersal of the intestines during the periods that the patient is lying down, a feature which appears helpful in correcting the constipation, (Fig. 2b).

TABLE III

Name	Sex	Height	Greatest Previous Weight	Weight at Institution of Regimen	Last Recorded Weight	Degree of Clinical Improvement
D.R.	F	5'1"	120 lb.	90 lb.	122 lb.	Excellent
M.M.	F	5'0"	140 lb.	83 lb.	94½ lb.	Good
H.B.	F	5'2"		83 lb.	136½ lb.	Excellent
H.G.	F	5'7"		101 lb.	124½ lb.	Excellent
F.D.	F			97 lb.	102 lb.	Fair
H.S.	F	5'1"	106 lb.	77½ lb.	94½ lb.	Good
C.F.	F	5'2"	125 lb.	96 lb.	133 lb.	Excellent
F.B.	F	5'6"	158 lb.	140 lb.	150 lb.	Good
M.S.	F	5'6"	125 lb.	110½ lb.	136 lb.	Good
C.T.	F	5'7"	140 lb.	112 lb.	140 lb.	Excellent

The improved nutrition was paralleled by fair to excellent clinical improvement in each of 10 of the more severe cases of undernutrition complicating generalized visceroptosis. All but D.R. were subjects of longstanding intractable undernutrition.

4. Exercises, aimed at improving the tone of the abdominal muscles, are carried out twice daily. We prefer that the patient, in this manner provide a natural abdominal support which is infinitely preferable to mechanical supports. The latter, in general, we believe may be useful for the patient too old to perform the prescribed exercises. Mechanical supports used exclusively prevent, rather than aid in improving the tone of the abdominal muscles.

Increased physical activity is encouraged after a normal appetite has been restored.

Clinical improvement parallels the gain in weight with remarkable regularity. The gain in weight is tangible proof to the patient that the improvement is real. Also, the basal metabolic rate, formerly slightly to moderately depressed, rises to normal and normal quantities of the 17 ketosteroids appear in the urine. The neuroses yield to reassurance when this is backed up by objective and subjective clinical improvement. This is not a problem for psychiatrists. Little will be gained in this group of patients by psychotherapy without appreciation of the existing physical disturbances and dietary measures needed for their improvement. We are emphatic that the reassurance in these cases should be from the internist.

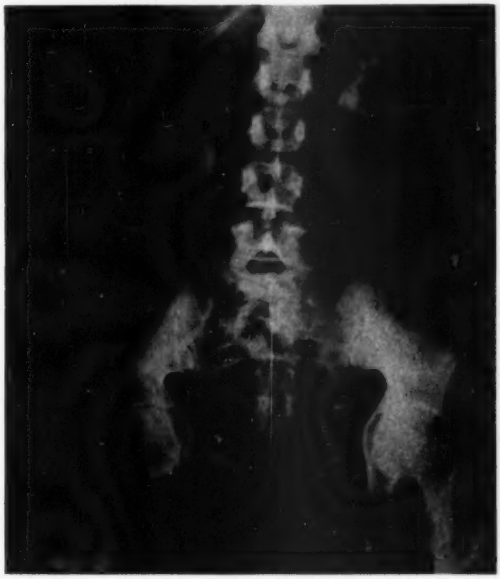


Fig. 3—The kinking of the ureter as frequently observed in the undernourished visceroptotic patient when studied in the upright position.

The improvement in nutrition in 10 of these patients is indicated in Table III and the general clinical improvement in 3 hitherto refractory cases is illustrated in the case records which follow.

Case 1:—C. T., female, aged 52, 5′7″ in height and weighed 113 pounds (April, 1948). Her complaints were: exhaustion, profound weakness, with threatened "blackouts" before breakfast, nausea after eating, and intractable constipation. She was obliged, because of fatigue, to stay in bed until 11 A.M., to rest between 2 and 4 P.M., and to retire at 6:30 P.M. These symptoms were precipitated following a loss of weight from 140 to 113 pounds due to voluntary restriction in diet.

She was admitted to the hospital for initial treatment and training. The diet specifically provided 150 grams of protein and 3,500 calories and comprised three small meals at the regular meal time with liquid formula between meals and at bed time.

This patient exhibited the usual anxiety state, with the firm conviction that she would always be an invalid and that she would never be able to gain in weight *because many doctors had failed in the attempt.* She exhibited the physical evidences of undernutrition and visceroptosis.

The foot of the bed was raised six inches and she was instructed to lie down, with the feet thus elevated, for one-half hour after each meal.

A gain in weight promptly ensued, her symptoms gradually subsided, and within two months she was, as she stated, a "new woman". When seen in June, 1951, she was going at a "terrific pace", had recently put on a big party for her two children home from college, had a happy sparkle in her eye—an observation made to me by her husband—and she weighed 140 pounds—a gain of 27 pounds.

Case 2:—M. M., a 37 year-old unemployed white woman, was admitted to the Pennsylvania Hospital through the Benjamin Franklin Clinic in March, 1949, with the chief complaints of dull, aching lower abdominal pain, anorexia, weakness, and constipation of approximately nine years' duration. There was a past medical history of colitis of unspecified type, a left nephropexy, severe dysmenorrhea, and nervousness. Her best weight had been 140 pounds at the age of 17, followed by a gradual loss of weight until the onset of the chief complaints after which she lost weight more rapidly. During the three weeks immediately prior to entry she developed headache, intractable vomiting, severe constipation, and further precipitate loss of weight.

On entry the patient weighed 83 pounds (36.9 kg.) and measured 60 inches (150 cm.) in height. The positive findings on physical examination included marked wasting, dry flaccid skin, small atrophic breasts, poorly localized abdominal tenderness, a palpable but otherwise unremarkable liver edge and lower pole of the right kidney, bulging of the lower abdominal wall with the patient in the erect position (Fig. 1), and generalized hyperesthesia.

Barium studies of the upper and lower gastrointestinal tracts revealed a marked degree of generalized visceroptosis.

The regimen, for patients with visceroptosis complicated by undernutrition, of diet, position, and exercises was instituted. For the first three weeks her con-

dition improved but little; however during the next two weeks her appetite improved markedly, she gained 11½ pounds in weight, and she changed from a taciturn, resigned semi-invalid into a cheerful, ambulant, outgoing person.

Case 3:—D. R., a 27 year-old white housewife, was relatively well until September, 1950, when she noted the onset of polyphagia, polyuria, weakness, dizziness, blurring of vision, and loss of weight. A urinalysis revealed glycosuria. A low calorie, low carbohydrate diet was prescribed by her physician. A loss of more than twenty pounds ensued, accompanied by further visual difficulties and the development of anorexia, weakness, amenorrhea, and severe constipation. Glycosuria continued and she was referred to the Pennsylvania Hospital for control of her diabetes mellitus.

The physical examination revealed a dehydrated, malnourished young adult woman weighing 90 pounds (40 kg.) and measuring 61 inches (152 cm.) in height. The positive findings included flaccidity of the skin, soft eyeballs, and moderate smoothness and redness of the tongue. The edge of the liver and the lower pole of the right kidney were easily palpable.

Examination of the blood revealed hyperglycemia and ketosis. After appropriate therapy with insulin and intravenous fluids, the diabetes was brought under control. Her body weight was 92 pounds. Roentgen-ray studies of the gastrointestinal system revealed generalized visceroptosis and atonicity of the intestines. In the erect position the patient's lower abdomen protruded markedly and was firm on palpation.

In addition to the diabetic regimen, the plan of therapy for undernutrition complicating visceroptosis was instituted. She was discharged from the hospital weighing 96½ pounds and feeling considerably better in all respects. She has been followed for the ensuing four months, during which time her weight has stabilized at 120 pounds, her constipation has disappeared, regular menses have been re-established, and she feels well. She is a cheerful happy housewife for the first time in years—and I might add a more grateful patient would be *difficult to find*.

In conclusion, we wish (1) to draw attention to the fact that there are a great number of visceroptotic persons who suffer from malnutrition; (2) to make a plea for consideration of the part which malnutrition plays in the fatigued, underweight, constipated, visceroptotic patient; (3) to emphasize the importance of examining these patients in the erect as well as in the recumbent position; (4) to indicate the simple means of detecting the visceroptosis which we believe plays a great part in preventing restoration to normal well-being without special measures; (5) to present a plan of therapy which we have found to be highly effective in the treatment of this oft neglected, overstudied, and sad

group of patients. These measures are commended for trial and it is recommended that they be heavily tinctured with enthusiasm and reassurance. Above all, it has been found that a careful follow through on the diet prescribed is essential to success and that to attempt the initial phase of treatment without hospitalization is futile.

Finally, we believe that many individuals are subjects of asymptomatic visceroptosis, but that a rapid loss in body weight in these individuals is corrected with greater difficulty than in those in whom there is no visceroptosis. We conclude, therefore, that visceroptosis predisposes to the maintenance of malnutrition and that for its correction special measures are essential.

Discussion

Dr. C. J. Tidmarsh (Montreal, Canada):—I think we should be grateful to Dr. Duncan for bringing to our attention a much neglected condition which affects us as gastroenterologists, and particularly for presenting to us a very common sense approach to this subject. I think we can all recall—perhaps not all, but some of us can recall—twenty or twenty-five years ago when these sad patients were referred to as "ptotic neurotics", and little or nothing was done for them.

In many instances, as Dr. Duncan has said, overtreatment, overenthusiasm, led to further invalidism and often with fatal results.

There is no question about it that these patients should not become too impressed with their illness and therefore that little attention, as little attention as possible, should be directed toward that angle. The reassurance, the rest in the hospital, the diet, and particularly the exercise, as Dr. Duncan pointed out, have proven in my experience the only successful method of approach to this group of patients. Vitamins, injections, the use of these supporting abdominal belts—all these have no place in the therapy of this group of cases.

I was interested in hearing Dr. Duncan say that perhaps visceroptosis in a subclinical state may influence the functioning of the digestive tract. We see a great many patients with constipation of one sort or another, and some of us are impressed at times by the extreme degree of atonicity of the colon with ptosis. Some have thought (and I think I have thought) that the position of the colon has really little to do with this function. In other words, I was of the impression that the colon would function even though it were placed low in the abdomen. There may indeed be something in what Dr. Duncan has said this morning in regard to ptosis in relation to digestive function, something that we should perhaps investigate a little further.

As I said before, I, for one, am very grateful to Dr. Duncan for bringing to our attention this very excellent paper.

Dr. Garfield G. Duncan (*Philadelphia, Pa.*):—I wish to thank the discussers for their remarks. In answer to them, I would point out that it has been estimated that nearly a quarter of the general population have some degree of visceroptosis. It would appear that this anatomical configuration causes no disability in most cases. This is certainly true of the well nourished individuals in this group. However, if the patient with generalized visceroptosis loses weight rapidly, it is highly probable that the usual attempts to regain weight will not be successful and that a chronic state of malnutrition with substandard health and eventually an anxiety state will ensue.

I would like to re-emphasize first, that generalized visceroptosis becomes a clinical problem when the subject becomes malnourished and second, that the restoration of a normal state of health is the rule when the measures which I have outlined are conscientiously applied.

TREATMENT OF INTESTINAL INFECTIONS ASSOCIATED WITH LOW GRADE PATHOGENIC BACTERIA*†

ALBERT MILZER, M.D., Ph.D.

HELEN MacLEAN, B.S.

and

NAOMI McELWAINE, B.S.

Chicago, Ill.

Many studies have been made of the normal bacterial flora of the gastrointestinal tract. Most authorities regard the constituent flora in the average adult in order of frequency as follows: Gram negative coliform bacilli (*Escherichia coli* and *Aerobacter aerogenes*), the enterococcus (*Streptococcus fecalis*), staphylococci, Clostridia, *Bacteroides*, yeasts and occasional aciduric bacteria (*Lactobacillus acidophilus* and *L. bifidus*)[1-4]. Normally, the stomach is relatively sterile and only small numbers of bacteria are present in the upper part of the small intestine. The numbers and species of bacteria in the small intestine progressively increases distally, and the maximum number are found in the colon. The normal intestinal flora function as useful commensals which synthesize vitamins and decompose proteins and carbohydrates.

In addition to the above microorganisms, certain other species such as paracolon, *Proteus*, *Pseudomonas aeruginosa* and *Shigella alkalescens* are occasionally isolated from the intestinal tract of individuals with gastrointestinal complaints as well as from apparently normal persons. Clinicians are generally inclined to regard these species as part of the normal intestinal flora or of no etiologic importance in gastrointestinal infections. In fact many diagnostic laboratories fail to report the presence of these species in their routine stool examinations. There is increasing evidence in the literature, however, that certain of these species on occasion may be of etiologic significance, especially if present in predominate numbers in patients with gastrointestinal disease in which the usually recognized intestinal pathogens cannot be demonstrated. Some of the data in this paper tend to substantiate this latter point of view. This study is based on routine stool examinations of 5,880 unselected patients and employees of Michael Reese Hospital during the year 1950.

Materials and Methods

Most stool specimens were examined within one-half hour after passage and cultured routinely on SS agar, Endo agar plates and Selenite-F enrichment broth.

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From the Department of Bacteriology and Virology, Medical Research Institute, Michael Reese Hospital, Chicago, Ill.

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The Selenite-F enrichment broth was incubated at 37° C. for 18 hours and subcultured to bismuth sulfite agar. Isolated colonies were picked and identified in the usual manner by inoculation of various carbohydrate media, IMViC media, urea broth and nutrient gelatin. Serologic tests were carried out when indicated. Blood plates were also inoculated with specimens from patients with ulcerative colitis and newborn infants with diarrhea.

All stools were also simultaneously examined for parasites by Walter Sokniewicz using the direct smear, zinc sulfate flotation concentration and a modified hematoxylin-staining technic. Occasional specimens were cultured in Balamuth's media.

In vitro sensitivity tests for the antibiotics studied were performed by the serial tube dilution method using a slight modification of Kolmer's technic[5]. The *in vitro* sulfonamide sensitivity test used is an unpublished screen test developed by one of us (H.M.). This test is employed routinely at Michael Reese Hospital to determine *in vitro* sensitivity to sulfadiazine, sulfathiazole or gantrisin. Nutrient or blood agar plates are prepared containing a final concentration of 100 mg. per cent of the soluble salt of the test sulfa drugs. The sulfa plates together with a control plate are inoculated with 0.05 c.c. of a 1:1000 or 1:10,000 dilution, depending on the density of growth, of a 6 hour broth culture of the test organism. The plates are incubated at 37° C. for 24 hours, and the relative degree of inhibition is noted by comparing the amount of growth on the sulfa with the control plates.

Throughout this study sulfasuxidine was given orally in divided doses varying from 8 to 10 grams daily for a period of 7 to 10 days. The soluble sulfonamide drugs such as sulfadiazine or gantrisin were given orally in the dosage recommended by the manufacturer. Pediatric cases were given doses of 1 to 1½ grains per pound body weight of sulfonamides per 24 hours in equally divided amounts every 4 hours. The usual adult dosage for dihydrostreptomycin was 2 grams daily in equally divided doses by the oral route for 5 days. The pediatric dose was 100,000 to 200,000 units orally every 3 to 6 hours for 5 days. Longer periods of streptomycin therapy were discouraged because of the ease with which bacteria are known to develop resistance to this antibiotic. Patients were not considered cured unless the symptoms subsided, and a minimum of 2 or 3 stools taken at weekly intervals after stopping therapy were negative. Additional follow-up stools were obtained whenever possible. Terramycin was not available during most of this study.

Results

Results are based on routine stool examinations of 5,880 individuals during 1950 at Michael Reese Hospital. Of this number 1,880 were various hospital employees including nurses who reported no specific gastrointestinal complaints.

The pediatric cases numbered 1,440, while the remaining 2,560 were adult patients in the hospital or outpatients. At least one stool was examined for each adult and an average of 3 stools per child. Table I summarizes the positive bacteriological and parasitological findings.

While it is not the primary purpose of this paper to discuss the findings of the recognized intestinal pathogens, we believe it of interest to note that 9 or 34.6 per cent of the 26 individuals positive for Salmonella had no clinical signs or symptoms of infection. The species* of Salmonella isolated were as follows: S. *barielly*, 12; S. *give*, 4; S. *oranienburg*, 4; S. *javiana*, 1; S. *typhimurium*, 2; S. *montevideo*, 2; *and* S. *enteritidis*, 2.

The finding of only 5.5 per cent positive for *E. histolytica* is a rather low incidence for this area. Perhaps this low figure can be explained by the fact that over 25 per cent of the individuals studied were children, and the incidence of amebiasis is known to be considerably less in children[6]. Approximately 25 per

TABLE I

BACTERIOLOGICAL AND PARASITOLOGICAL FINDINGS IN ROUTINE STOOL EXAMINATIONS OF 5,880 INDIVIDUALS

	No. Positive	*% Positive*
Endameba histolytica	327	5.5
Salmonella spp.	26	0.44
S. *typhosa*	1	0.016
Paracolon	426	7.2
Proteus mirabilis	268	4.5
Proteus morganii	167	2.8
Shigella spp.	44	0.74
Pseudomonas aeruginosa	287	4.9
Total	1,546	26.096

cent of the adult cases were asymptomatic carriers. In the past we and others[7] have found that the incidence of amebiasis in the normal adult population in Chicago is closer to 10 per cent.

Of the 44 positive Shigella cultures, 38 were positive for S. *alkalescens* (type I), 2 were positive for S. *alkalescens* (type III), 2 S. *paradysenteriae* (Boyd 103) and 2 S. *paradysenteriae* (Flexner W and Z) respectively.

PARACOLON

As shown in Table I, 426 or 7.2 per cent of the stool specimens examined were positive for paracolon organisms. Of the 426 strains studied, 331 or 77.6 per cent were isolated from asymptomatic individuals or patients with no complaints referable to the gastrointestinal tract, 94 per cent of whom were adults. Ninety-five strains of paracolon or 22.4 per cent were isolated from individuals

*We are indebted to Dr. H. J. Shaughnessy of the Illinois Dept. of Public Health for the Salmonella typing.

with various gastrointestinal complaints. Of the latter group, 2 were also simultaneously infected with *S. barielly*, 3 with *Proteus mirabilis*, 1 with *Pseudomonas aeruginosa*, 3 with *Endameba histolytica* and 1 with *Giardia lamblia*. Thus a total of 85 individuals or approximately 20 per cent had gastrointestinal complaints in which a paracolon organism was the only potential pathogen isolated from the stool specimen.

Table II shows the results of *in vitro* sensitivity tests of 263 recently isolated strains of paracolon organisms. Results of streptomycin sensitivity are expressed in micrograms per c.c. necessary to inhibit growth. The sulfa drug screen test indicates whether there is complete, partial, or no inhibition of growth. The average sensitivity of the strains studied was 5 micrograms per c.c. for streptomycin, complete inhibition of growth by sulfathiazole and partial inhibition by sulfadiazine.

Table III summarizes the results of antibacterial therapy of 85 patients with various gastrointestinal complaints in which no known intestinal pathogens were isolated from the stool except the paracolon organism. The average percentage

TABLE II

IN VITRO SENSITIVITY OF 263 RECENTLY ISOLATED STRAINS OF PARACOLON BACILLI

Streptomycin Mcgm./c.c.				Sulfathiazole			Sulfadiazine		
0.625-10	20	40-80	>80	Complete Inhib.	Partial Inhib.	No. Inhib.	Complete Inhib.	Partial Inhib.	No. Inhib.
194	33	32	4	164	89	10	77	151	35

of paracolon colonies on Endo agar or SS agar plates in the 85 patients studied was 75 per cent; in 120 control individuals without gastrointestinal symptoms it was 23.16 per cent. Seventy-five per cent of the patients with acute gastroenteritis were children (chiefly under 5 years), while the reverse was true in the other categories of gastrointestinal complaints, except those with spastic colitis. The latter were all adults.

As shown in Table III approximately 94 per cent of the patients with paracolon infections were treated successfully with oral sulfonamides and/or dihydrostreptomycin. Most of the cases were given sulfasuxidine. About one-fourth of the cases treated successfully with sulfonamides were given sulfadiazine or gantrisin. Patients were not considered cured unless the symptoms subsided, and 2 or 3 stools taken at weekly intervals after stopping therapy were negative for paracolon. In this series there was a correlation between results of in vitro sensitivity tests for sulfonamides or streptomycin and therapeutic effect in most instances.

Seven patients with a diagnosis of functional spastic colitis were studied. One was successfully treated with sulfasuxidine, and one with dihydrostreptomy-

cin as indicated in Table III. Five received no antibacterial therapy because the clinician regarded the presence of paracolon in the stool of no significance. Two of the latter group were reported improved without specific therapy, while three were discharged with no improvement. Follow-up stools were not submitted from these patients except the two who were successfully treated with sulfasuxidine and streptomycin.

Table IV shows that approximately ninety-two per cent of the paracolon organisms isolated from patients with acute gastroenteritis were similar to biotype 32011 (aerobacter) paracolon recovered by Stuart and Rustigian[8] from known gastroenteritis patients. Most of the strains isolated from patients in the other categories of clinical diagnoses were paracolons of the coli or intermediate type. On the other hand, approximately 60 per cent of the paracolon strains isolated from asymptomatic individuals were the coli type, 35 per cent the intermediate type and only 5 per cent were similar to biotype 32011 (aerobacter) paracolon.

TABLE III

ANTIBACTERIAL THERAPY OF 85 PATIENTS WITH VARIOUS GASTROINTESTINAL COMPLAINTS ASSOCIATED WITH PARACOLON BACILLI

Diagnosis	Number	Cured or Improved by			
		Sulfa Drugs	Dihydrostreptomycin	Combinations*	None
Acute Gastroenteritis	39	23	6	10	—
Chronic Gastroenteritis	25	12	8	5	—
Chronic Diarrhea	14	11	—	3	—
Spastic Colitis	7	1	1	—	5**

* Sulfa drug plus dihydrostreptomycin
** 3 not cured

The following case histories illustrate the role of paracolon in certain gastrointestinal infections and the successful therapy of such infections with sulfonamides and/or dihydrostreptomycin.

PARACOLON CASE REPORTS*

Case 1:—F. R., a 6½ month old premature male infant was admitted with a diagnosis of infectious diarrhea of 7 days' duration, a low grade temperature, and vomiting after feeding for 2 days. He passed numerous greenish watery stools daily. Physical examination was essentially negative. Stool cultures revealed the presence of practically 100 per cent paracolon colonies on Endo and SS agar plates. The isolated strain was completely inhibited in the *in vitro* screen test by sulfadiazine and partially inhibited by sulfathiazole. It was sensitive to 20 micrograms per c.c. of streptomycin. The patient was treated with a com-

*We are indebted to Drs. J. Greengard, J. Schlichter and I. Mack for permission to study their patients.

bination of cremosuxidine, one ounce every four hours, and oral streptomycin, 100,000 units orally every 4 hours for a total of 6 days. The diarrhea diminished within 3 days after onset of therapy, and the stools became normal on the fifth day at which time the patient was also afebrile. Three stool cultures taken at weekly intervals after therapy was stopped were negative.

Case 2:—H. T., a 31 year old white male, was admitted to the hospital with bloody diarrhea and abdominal cramps of 2 days' duration. He had a history of malaria and hookworm infestation 4 years previously. The latter was apparently cured by tetrachloroethylene. On physical examination tenderness in the lower left quadrant of the abdomen was noted. Sigmoidoscopic examination revealed a hyperemic mucous membrane with no evidence of ulceration. Other findings were normal. Cultures of the stool revealed 90 per cent paracolon colonies on Endo and SS agar plates. Cysts of *Endolimax nana* and trophozoites of *Dientameba fragilis* were also seen in wet preparations of the stool. The paracolon

TABLE IV

CLASSIFICATION OF PARACOLON STRAINS ISOLATED FROM PATIENTS WITH VARIOUS INTESTINAL SYMPTOMS AND ASYMPTOMATIC INDIVIDUALS

Diagnosis	No. of Strains	Paracolon Types		
		Biotype 32011	Coli	Intermediate
Acute Gastroenteritis	39	36	2	1
Chronic Gastroenteritis	25	5	10	10
Chronic Diarrhea	14	3	6	5
Spastic Colitis	7	1	4	2
Asymptomatic	164	8	100	56

strain was sensitive to 2.5 micrograms per c.c. of streptomycin, and growth was completely inhibited by sulfathiazole and partially inhibited by sulfadiazine in the screen test. The patient was treated with 2.5 grams of sulfasuxidine five times daily for 17 days. He was also given diodoquin, 9.6 grains, 3 times daily for 10 days. His diarrhea and abdominal cramps cleared up within 7 days after starting treatment. Stools examined 17 days after-treatment was stopped were negative for paracolon and the amebae.

Case 3:—S. L., a 63 year old female, was admitted in congestive heart failure. She had a history of orthopnea and dyspnea of 3 months' duration. After she was in the hospital for 8 days her congestive failure was controlled by digitoxin, but she developed a diarrhea and abdominal discomfort. Sixty per cent paracolon colonies were noted in stool cultures on Endo and SS agar plates. The isolated strain was sensitive to 0.625 micrograms of streptomycin per c.c. and growth was completely inhibited by sulfathiazole and sulfadiazine in the screen test. The patient was treated with 1 gram of oral streptomycin daily for 5 days and gantrisin starting 4 days later. She was given 1 gram of gantrisin every 4 hours daily for 4 days. The diarrhea and abdominal discomfort disappeared after 4 days of

treatment, although she continued to receive digitoxin. Stools collected one, two and four weeks after starting treatment were negative. She was discharged improved with no gastrointestinal complaints 6 weeks after admission and transferred to a convalescent home.

Case 4:—M. E., a 50 year old colored female, was admitted with a diagnosis of rheumatoid arthritis and enteritis. She had diarrhea for the past 3 months and dated the onset of enteritis to a Thanksgiving dinner. Eighty per cent paracolon colonies was isolated from her stools. Physical examination revealed epigastric tenderness as well as the findings of rheumatoid arthritis. *In vitro* sensitivity tests showed that the isolated strain was sensitive to 20 micrograms per c.c. of streptomycin and growth was inhibited by sulfathiazole and partially by sulfadiazine and gantrisin. The patient was treated with gantrisin 1 gram every 6 hours for 4 days and then with sulfathalidine 2 grams every 4 hours for 11 days. The patient's gastrointestinal symptoms disappeared on the fifth day of treatment, and 3 successive stools collected at weekly intervals after stopping the sulfonamides were negative.

TABLE V

IN VITRO SENSITIVITY OF 144 RECENTLY ISOLATED STRAINS OF *Proteus mirabilis* AND 108 STRAINS OF *Proteus morganii*

Organism	Streptomycin Mcgm./c.c.				Sulfathiazole			Sulfadiazine		
	0.625-10	20	40-80	>80	Complete Inhib.	Partial Inhib.	No Inhib.	Complete Inhib.	Partial Inhib.	No Inhib.
P. mirabilis	66	53	21	4	99	42	2	121	20	2
P. morganii	67	34	6	1	97	11	0	101	7	0

Case 5:—M. C., a 28 year old female, was admitted with a diagnosis of acute appendicitis. She had a history of lower abdominal pain of 4 days' duration. Physical examination revealed tenderness of the lower part of the abdomen, but, it was not possible to localize the pain. An intravenous pyelogram was negative. An appendectomy was performed without relief of symptoms. In the meantime a stool examination showed the presence of 40 per cent paracolon colonies. The isolated strain was sensitive to 10 micrograms of streptomycin per c.c., and growth was completely inhibited by sulfathiazole and partially by sulfadiazine. She was given sulfasuxidine 2 grams every 4 hours, but had to stop after 3 days of therapy due to drug intolerance. She received a total of 36 grams of sulfasuxidine. Her abdominal symptoms disappeared on the third day of therapy, and stools collected one and six weeks after stopping treatment were negative.

PROTEUS

There is much less evidence that members of this genus may be human pathogens than for the paracolon group[9]. Of the 435 strains isolated in this series (Table I), 268 were *P. mirabilis* and 167 *P. morganii*. Fifty-five or 20.5 per cent of the *P. mirabilis* strains were isolated from patients with various gastrointestinal symptoms, chiefly mild diarrheas in children. This number does

not include the following patients with mixed infections: five with *E. histolytica*, 3 with *P. morganii*, 1 with *G. lamblia*, 4 with paracolon and 1 with typhoid. The majority of patients with diarrhea (73.5 per cent) associated with *P. mirabilis* in stool cultures occurred following recent antibiotic therapy with penicillin, aureomycin or chloromycetin. It is well known that most strains of *Proteus* are resistant to these antibiotics[10].

Only 18 or 10.8 per cent of *P. morganii* strains were isolated from patients with diarrhea. Thirty per cent of the latter strains were isolated following recent antibotic therapy with penicillin, aureomycin or chloromycetin. Like *P. mirabilis* most of the *P. morganii* strains were isolated from children. One patient was also simultaneously infected with *E. histolytica* and another with *Pseudomonas aeruginosa*.

The results of *in vitro* sensitivity tests of the *Proteus* species are shown in Table V. It is difficult to evaluate antibacterial therapy of diarrhea associated with *Proteus* because in our experience these organisms tend to disappear spontaneously from the stool within one to two weeks after onset of symptoms without specific therapy. Furthermore, we found no significant difference in percentage of *Proteus colonies* isolated from patients with gastrointestinal symptoms and others with none. The following 3 case reports indicate that diarrheas associated with *Proteus* apparently may be successfully treated with sulfonamides and/or streptomycin but are inconclusive because as already mentioned such diarrheas often disappear without therapy.

Proteus Case Reports*

Case 6:—M. B., a 29 year old white male, was admitted with a history of diarrhea of 2 months' duration and severe headache of 3 days' duration. Cultures of the stool revealed 100 per cent *P. mirabilis* colonies. The isolated organism was sensitive to 1.25 micrograms per c.c. of streptomycin and growth was completely inhibited by sulfadiazine, sulfathiazole and gantrisin. The patient was treated with sulfadiazine, 1 gram four times daily, for one week. The diarrhea diminished on the third day, and a stool collected one week after therapy was stopped was negative, but the patient relapsed one month later. This time stool cultures showed 90 per cent *P. mirabilis* colonies, and a second course of sulfadiazine in the same dosage as previously was given. The stools became normal on the fifth day after therapy was started and were negative one and two weeks later. Two additional stools collected 2 and 3 months after the second course of therapy were also negative for *P. mirabilis*.

Case 7:—B. G., a newborn white male, was delivered by section and treated with crystacillin, 100,000 units daily because of congenital heart disease. The

*We are indebted to Drs. J. Schlichter, J. Greengard and R. H. Kunstadter for permission to study their patients.

infant developed a severe diarrhea on the sixth day of penicillin therapy, and 60 per cent *P. mirabilis* colonies were noted in cultures of the stool. The isolated strain was sensitive to 5 micrograms per c.c. of streptomycin and growth was completely inhibited by sulfadiazine, sulfathiazole and gantrisin. The baby was treated with oral dihydrostreptomycin 0.1 gram every 3 hours and cremothalidine 20 drops three times daily for one week. The stools were normal one week after stopping therapy and negative for *P. mirabilis*. Additional stool specimens were not submitted to the laboratory.

Case 8:—P. F., a 12 week old white female, was admitted with a history of diarrhea, irritability and low grade temperature of 12 days' duration. Her stools were watery and green. Stool cultures showed 90 per cent *P. mirabilis* colonies, and the same species was also isolated from the urine. The isolated strains were sensitive to 5 micrograms per c.c. of streptomycin, and growth was completely inhibited by sulfadiazine and sulfathiazole. The patient was treated with oral chloromycetin 50 milligrams every 3 hours and dihydrostreptomycin 125 milligrams every 6 hours for 7 days. The stool became normal on the seventh day of treatment, and catheterized urine and stool cultures taken one week after therapy was completed were negative for *P. mirabilis*. A follow-up stool culture taken one month later was also negative.

TABLE VI

IN VITRO SENSITIVITY OF 39 RECENTLY ISOLATED STRAINS OF *Shigella alkalescens*

Streptomycin Mcgm./c.c.			Sulfathiazole			Sulfadiazine			Chloromycetin Mcgm./c.c.		Terramycin Mcgm./c.c.
0.625-10	20	40	Complete Inhib.	Partial Inhib.	No Inhib.	Complete Inhib.	Partial Inhib.	No Inhib.	2	4-6	2-8
24	14	1	37	2	1	23	15	1	17	15	16

SHIGELLA

Forty-four or 0.74 per cent of the stool cultures examined were positive for *Shigella* (Table I). Of this number 38 strains were identified as *S. alkalescens* (type I) and 2 *S. aklalescens* (type III). Ten strains of type I were isolated from 6 adults and 4 children with gastroenteritis. None of these patients had received any antibiotics or sulfonamides prior to onset of symptoms. The remaining 29 strains were isolated from asymptomatic individuals, including 2 patients with simultaneous *E. histolytica* infection. The results of *in vitro* sensitivity tests of the isolated 39 strains are shown in Table VI.

Four of the 10 patients with gastroenteritis were successfully treated with sulfadiazine, one with sulfasuxidine, three with chloromycetin, and one failed to respond to sulfadiazine and sulfasuxidine but was cured by streptomycin. The tenth patient was a 13 year old male who failed to respond clinically or bacteriologically to sulfasuxidine, chloromycetin or terramycin but was cured with poly-

myxin B. This case is especially interesting because the isolated strain of *S. alkalescens* was sensitive to all of these drugs *in vitro*. He was treated with 150 mg. of polymyxin B every 4 hours, orally, omitting the night dose for 5 days. A stool specimen obtained on the seventh day after treatment was begun was negative for *Shigella*. Two subsequent stool cultures taken one and a half months after polymyxin therapy were also negative for *Shigella*. Further details of this latter case are described elsewhere[11]. The following are a few typical case reports.

Shigella Case Reports*

Case 9:—H. J., a 42 year old white male, was admitted with a history of diarrhea and slight abdominal tenderness for the past 2 weeks. His stool was cultured and 95 per cent of the isolated colonies were *S. alkalescens*, type I. The isolated strain was sensitive to 20 micrograms per c.c. of streptomycin and 4 micrograms per c.c. of chloromycetin. There was complete inhibition of growth by sulfathiazole and partial inhibition by sulfadiazine in the screen test. The patient was treated with chloromycetin 500 mg. every 6 hours for 5 days. On the fourth day his stool became normal, and specimens collected one, two and four weeks after completion of therapy were negative for *Shigella*.

Case 10:—D. H., a 45 year old white female, had a history of diarrhea and cramps of 3 days' duration. Stool culture revealed eighty per cent *S. alkalescens* type I colonies. Growth of the isolated strain was completely inhibited by sulfathiazole and sulfadiazine in the screen test. It was sensitive to 5 micrograms per c.c. of streptomycin and 2 micrograms per c.c. of both chloromycetin and terramycin. The patient was treated with sulfadiazine in the usual dosage for 7 days. Her stools became normal and the cramps disappeared on the third day of therapy. The stool cultures were negative for *Shigella* one, two and three weeks after stopping therapy.

Case 11:—D. L., a 91 year old white female, had a history of diarrhea and abdominal cramps of two weeks duration. She had lost 8 pounds. Stool cultures revealed 70 per cent *Shigella alkalescens* type I colonies. The isolated strain was sensitive to 40 micrograms per c.c. of streptomycin, and 6 micrograms per c.c. of chloromycetin. Growth was partially inhibited by sulfadiazine and completely by sulfathiazole. The patient was treated for 7 days with the usual dosage of sulfadiazine and then sulfasuxidine for 7 days but failed to respond. She next received oral dihydrostreptomycin 2 grams daily combined with sulfasuxidine for one week followed by an additional 3 weeks of dihydrostreptomycin alone. Her diarrhea and cramps diminished during the second week of streptomycin therapy, and the stools became normal. Stool cultures made two and four weeks after completion of therapy were negative for *Shigella*.

*We are indebted to Drs. J. Sloan, S. Schwartz and H. Sorter for permission to study their patients.

Pseudomonas

Two hundred and eighty-seven or 4.9 per cent of the stool cultures were positive for *Pseudomonas aeruginosa* (Table I). Of this number 44 strains or 15.3 per cent were isolated from patients with gastrointestinal complaints, chiefly gastroenteritis or mild diarrhea in which the *Pseudomonas* was the only potential pathogen isolated. Twenty-three strains were isolated from patients with gastroenteritis, 19 strains from cases with diarrhea and 2 from ulcerative colitis (Table VIII). Eighteen of the 23 patients with gastroenteritis were children, mainly under 1 year of age. Four of the five adults who were positive were debilitated and had a carcinoma in the intestinal tract. Fourteen of the 19 strains isolated from cases of diarrhea were children. The two cases of ulcerative colitis were a child of 4 years and an adult aged 29 years. The average percentage of *Pseudomonas* colonies in the stool cultures of patients with gastrointestinal symptoms was 72.5 per cent compared to 40 per cent in 50 asymptomatic individuals.

As in *Proteus infections*, the majority of *Ps. aeruginosa* strains isolated from patients with symptoms (81.9 per cent) occurred following recent therapy with antibiotics such as penicillin, aureomycin, chloromycetin or terramycin. Most

TABLE VII
In Vitro Sensitivity of 287 Recently Isolated Strains of *Pseudomonas aeruginosa*

Streptomycin Mcgm./c.c.				Sulfathiazole			Sulfadiazine			Polymyxin B Mcgm./c.c.
0.625-10	20	40-80	>80	Complete Inhib.	Partial Inhib.	No Inhib.	Complete Inhib.	Partial Inhib.	No Inhib.	0.1-2
44	42	87	26	184	5	26	184	5	26	40

strains of *Ps. aeruginosa* are resistant to these antibiotics *in vitro*[10]. The results of *in vitro* sensitivity tests of the recently isolated *Ps. aeruginosa* strains in this series are shown in Table VII.

Eight patients or 18.1 per cent with symptoms recovered without specific therapy and had negative stools 3 to 4 weeks later (Table VIII). On the other hand, the treated patients usually were well and had negative stools within one week after treatment was stopped. Nine patients responded to oral dihydrostreptomycin given in divided dosages of 2 grams daily for 5 days. Eighteen patients were treated successfully with combined sulfa drugs and oral dihydrostreptomycin. Four patients responded to the usual dosages of sulfadiazine, one to sulfathalidine and one to tricombusil. Three patients failed to respond to combined sulfa drugs and oral dihydrostreptomycin but responded to polymyxin B given orally. The oral dosage of the latter was 200 mg. three times a day for adults, and 2 mg. per kilogram of body weight every 6 hours for children. The polymyxin was given for 7 days. A previous paper[11] discusses successful polymyxin therapy of other cases of gastrointestinal infections associated with *Ps. aeruginosa*.

Pseudomonas Case Reports*

Case 12:—D. K., a 7 month old white male, was admitted with a history of diarrhea of two days duration. He vomited twice on the day of admission. Stool cultures revealed 80 per cent *Ps. aeruginosa* colonies. The isolated strain was sensitive to 20 micrograms per c.c. of streptomycin and growth was completely inhibited by sulfadiazine and sulfathiazole in the screen test. The patient was treated with 0.1 gram of dihydrostreptomycin orally every 4 hours for 5 days. The stools became normal on the third day of therapy and were negative for *Ps. aeruginosa* when cultured 2 and 3 weeks after completion of therapy.

Case 13:—R. S., a 31 month old white male, was admitted with a history of vomiting, diarrhea and fever up to 101° F. for 2 days. His stools consisted of mucus but no blood. There was occasional abdominal pain. The patient had received crystacillin for an upper respiratory infection for 5 days prior to the onset of the diarrhea. Stool cultures showed 90 per cent *Ps. aeruginosa* colonies. The isolated strain was sensitive to 40 micrograms per c.c. of streptomycin and growth was completely inhibited by sulfathiazole and sulfadiazine. The patient was treated with a combination of sulfadiazine 0.3 grams every 6 hours and oral dihydrostreptomycin 0.1 gram every 6 hours for 4 days. His stools and body temperature became normal on the fourth day and cultures taken one and four weeks after completion of therapy were negative for *Ps. aeruginosa.*

TABLE VIII

Antibacterial Therapy of 44 Patients with Various Gastrointestinal Complaints Associated with *Pseudomonas aeruginosa*

Diagnosis	Number	Cured or Improved by			Polymyxin	
		Sulfa Drugs	Dihydrostreptomycin	Combination*	B	None
Gastroenteritis	23	2	5	11	3**	2
Diarrhea	19	4	3	6	—	6
Ulcerative Colitis	2	—	1	1	—	

*Sulfa drugs plus dihydrostreptomycin.
**Failed to respond to previous sulfa plus streptomycin therapy.

Case 14:—L. L., a 4 week old white female, was admitted with a history of progressively increasing diarrhea during the past 10 days. Rectal temperature was 101° F. on admission. The stools were watery green with a few curds. Stool cultures revealed 50 per cent *Ps. aeruginosa* colonies. The isolated strain was sensitive to 40 micrograms per c.c. of streptomycin and growth was almost completely inhibited by sulfadiazine and sulfathiazole. The patient was given sulfadiazine 0.3 gram every 8 hours for 7 days. The stools became normal on the fifth day and were negative for *Ps. aeruginosa* when tested one, two and three weeks after completion of therapy.

*We are indebted to Drs. J. Greengard, L. Braun, and H. Sapoznik for permission to study their patients.

Case 15:—A. R., a 39 year old white male, was admitted with a history of colitis and diarrhea of 2 months and acute glaucoma. Ninety per cent of the stool culture colonies were *Ps. aeruginosa*. The isolated strain was sensitive to 40 units per c.c. of streptomycin and growth was completely inhibited by sulfadiazine and sulfathiazole. The patient was given tricombusil 1 gram every 6 hours for 12 days. The symptoms subsided and his stools became normal on the tenth day of therapy and were negative for *Ps. aeruginosa* on the first, second and third week after therapy was completed. A follow-up stool taken 8 months later was also negative for *Pseudomonas*.

Discussion

The paracolon bacteria are usually considered to lie between the coliform bacteria and the Salmonella. They may be defined as aerobic, nonsporulating, Gram negative rods which ferment glucose with formation of gas but are delayed lactose fermenters[4]. Occasional strains fail to ferment lactose.

Evidence continues to accumulate in the literature that certain strains of paracolon bacilli are pathogenic for man. Edwards et al[12] have reported that the so-called Arizona group of paracolon bacteria have pathogenic properties. Fifty-five types have been described. Recently Murphy and Morris[13] have described two outbreaks of gastroenteritis apparently caused by a paracolon of the Arizona group. Stuart and Rustigian[8] have evidence of the pathogenicity of another type of paracolon which they designated as "Biotype 32011"; eight serotypes of this latter strain have been identified. Members of Biotype 32011 have also been isolated by Barnes[14] from outbreaks of gastroenteritis affecting naval personnel. Another group of paracolon bacilli have been isolated by Stuart et al[15] in an epidemic of gastroenteritis in infants. Others have described strains of paracolon bacilli isolated from patients with gastroenteritis with *Salmonella* or *Shigella*[16] antigens. Paracolon bacteria have also been isolated from urinary tract infections[17], typhoid-like infections[18], endocarditis[19] and pneumonia[20].

The paracolon strains isloated in the present study were obtained from either asymptomatic individuals or sporadic cases of diarrhea or gastroenteritis. We feel that it is significant that the average percentage of paracolon colonies isolated on Endo or SS agar plates from patients with gastrointestinal symptoms was 75 per cent compared to 23.16 per cent in 120 asymptomatic individuals. Also the majority of patients with acute gastroenteritis were children under 5 years of age from whom a paracolon strain similar to biotype 32011 aerobacter of Stuart and Rustigian[8] was isolated. Three of 7 patients with functional spastic colitis who were given no specific therapy were discharged with no improvement. Two improved without therapy while one was cured with sulfasuxidine and the seventh with dihydrostreptomycin. In this connection it is of interest to note that Luippold[21] and Darnall[16] have described several cases of chronic enterocolitis

with systemic manifestations which were considered functional in origin because paracolon organisms and none of the usually accepted intestinal pathogens were noted. Streptomycin therapy in all these cases resulted in elimination of the paracolon bacilli and in clinical cure or improvement.

Most of the paracolon strains tested were sensitive *in vitro* to streptomycin or one of the sulfonamide drugs (Table II). The majority of our patients were treated successfully with oral sulfonamides and/or dihydrostreptomycin, and in most instances there was a correlation between *in vitro* sensitivity tests and clinical response. In our experience oral streptomycin is well tolerated in dosages of 2 grams daily and can be used successfully to treat patients with paracolon bacilli sensitive to 80 micrograms per c.c. Most of the patients treated with sulfonamides were given sulfasuxidine. We feel that an insoluble sulfonamide or oral streptomycin is the drug of choice for treatment of sensitive paracolon infections localized in the gastrointestinal tract because there is minimal absorption of these drugs from the intestine.

We have had no experience treating paracolon intestinal infections with the newer antibiotics such as chloromycetin, aureomycin, terramycin or polymyxin. As far as we know no publications on this subject have appeared to date. However, we have tested the *in vitro* sensitivity of 14 recently isolated paracolon strains and have found that most of them are sensitive to these antibiotics[10].

Although members of the genus *Proteus* have been isolated from cases of gastroenteritis their significance as enteric pathogens remains unestablished. Cherry et al[22] have presented circumstantial evidence of the etiologic relationship of *Proteus mirabilis* in an outbreak of gastroenteritis. Most workers, however, are reluctant to attribute any significance to the presence of these organisms in various intestinal infections. For example, Neter and Goodale[9a] feel that the pathogenic significance of Morgan's bacillus in summer diarrhea of children and other intestinal infections is doubtful. On the other hand, others[23] have indicated that *Proteus* is of etiologic significance in infant diarrhea on the basis of increased incidence in stool cultures. In our opinion such circumstantial evidence is inadequate to incriminate an etiologic agent because Koch's postulates have not been adequately fulfilled.

No conclusive evidence was obtained in the present studies implicating *P. mirabilis* or *P. morganii* as intestinal pathogens. We found no significant difference between the percentage of *Proteus* colonies isolated from cases with gastrointestinal symptoms and others with none. Most of the *Proteus* species associated with diarrhea in our series occurred in individuals who had received recent previous therapy with penicillin, aureomycin, chloromycetin or terramycin. At present it is a moot question as to whether *Proteus* is responsible for the diarrheas known to follow some of the broad-spectrum antibiotics or is merely

present in predominant numbers because the normal flora is inhibited. In any event we found that both the diarrhea and *Proteus* tend to disappear spontaneously without antibacterial therapy in about one to two weeks at which time the normal intestinal flora returns. Recent evidence indicates that moniliasis and/or alteration in vitamin biosynthesis may be responsible for the diarrhea following antibiotic therapy[24,25]. Treatment with Vitamin B-complex seems to have some therapeutic value. Stools were not cultured for monilia in the present study.

Like the paracolon group most of the *Proteus* strains isolated are sensitive to both streptomycin and the various sulfonamide drugs (Table V). A limited number of sensitivity tests with chloromycetin, aureomycin, polymyxin B and terramycin indicated that most of our strains of *Proteus* were resistant to these antibiotics. These findings are in agreement with those of others[26,27]. It is difficult to evaluate the antibacterial therapy of the 3 cases of diarrhea associated with *Proteus* which were presented because of the fact that such diarrheas are often self-limiting. On the other hand, Levinson and Raycraft[28] state that the average duration of diarrhea in children under one year of age associated with *Proteus* was cut from approximately five to three days by the use of etiher sulfadiazine or oral streptomycin.

The pathogenicity of the Shiga, Flexner, Sonne and Schmitz dysentery bacilli is well established, but some still regard S. *alkalescens* as nonpathogenic for man. Convincing evidence is accumulating, however, that this species may cause mild or even severe forms of dysentery or enteritis [28-30]. It may also cause septicemia and urinary tract infections[31,32]. Patients infected with S. *alkalescens* may develop specific agglutinins during the course of the disease[33]. Both Neter[34] and Weil[35] in their reviews of *Shigella* regard S. *alkalescens* as pathogenic, but point out that this species can often be isolated from the stools of asymtomatic individuals.

In our series most of the strains of S. *alkalescens* (75 per cent) were isolated from asymptomatic individuals, chiefly adults. The remaining 10 strains were isolated from 6 adults and 4 children with gastroenteritis. Clinically all of these cases were moderate in severity and had at least 70 per cent S. *alkalescens* (type I) colonies in their stool cultures. All of the 39 strains tested except one were sensitive to streptomycin and the sulfonamide drugs (Table VI). Most of these strains were also sensitive to chloromycetin, terramycin and polymyxin B[11].

Five of the 10 patients treated with sulfonamides responded both clinically and bacteriologically. All of these strains were sensitive to both sulfadiazine and sulfathiazole in the screen test. One patient (Case 11) failed to respond to a course of sulfadiazine followed by sulfasuxidine but was cured by oral dihydrostreptomycin. The strain of S. *alkalescens* isolated from Case 11 was only partially

inhibited by sulfadiazine but was sensitive to 40 micrograms per c.c. of streptomycin. Three patients were cured by chloromycetin. We are unable to explain why the tenth patient failed to respond to sulfasuxidine, chloromycetin or terramycin but was cured by polymyxin B although the isolated strain was sensitive *in vitro* to all these agents.

In a separate report[11] we described an additional case of diarrhea due to S. *alkalescens* which recovered clinically following a course of sulfadiazine, but the stool cultures became positive one week after stopping medication. The stool cultures subsequently became negative after a course of terramycin. At present sulfadiazine, chloromycetin, aureomycin, polymyxin B[11,36] and more recently terramycin[11] are all considered effective antibacterial agents in *Shigella* infections. More studies are needed, however, for the final evaluation of the newer antibiotics.

Pseudomonas aeruginosa is known to produce an acute or subacute enteritis with or without constitutional symptoms and diarrhea in both children and adults[37]. An epidemic of diarrhea of the newborn with a high mortailty has also been attributed to this organism[38]. On occasion a typhoid-like fever has been produced[39]. Stanley[37] has recently reviewed the incidence and serious prognosis of meningitis, endocarditis, pyelonephritis and other infections due to *Ps. aeruginosa*.

Forty-four or 15.3 per cent of the *Ps. aeruginosa* strains isolated in the present study were obtained from patients with gastroenteritis or mild diarrhea. Most of the patients with gastroenteritis were children under one year of age; the remainder were debilitated adults with intestinal carcinoma. The majority of patients with diarrhea were also children. The average percentage of *Ps. aeruginosa* colonies was significantly greater in stool cultures of patients with gastrointestinal complaints than in asymptomatic individuals. As in *Proteus* infections most of the *Pseudomonas* strains which were isolated from patients with symptoms followed recent therapy with penicillin, aureomycin, chloromycetin or terramycin. Possibly the present widespread uses of these antibiotics to which most strains of *Ps. aeruginosa* are resistant may explain the increased incidence of this species in the stool in recent years[37].

The majority of the strains which we isolated were sensitive to both sulfadiazine and sulfathiazole in the screen test and to streptomycin if one remembers that an organism confined to the intestinal tract with a sensitivity of 80 micrograms per c.c. can often be successfully treated with oral streptomycin. It should be emphasized, however, that the majority of the strains tested were resistant to more than 20 micrograms per c.c. and would, therefore, be too resistant for streptomycin therapy in systemic infections. Seventy-five per cent of the patients with intestinal symptoms were successfully treated with one of the sul-

fonamide drugs and/or oral dihydrostreptomycin and were cured clinically and bacteriologically within one to two weeks after onset. Eight patients who received no therapy required 3 to 4 weeks to recover and have negative stools. There was a correlation between results of *in vitro* sensitivity tests and clinical response in most of the cases. The 3 patients who failed to respond to combined sulfonamide and streptomycin therapy had resistant strains in the stool. The latter were cured with oral polymyxin B. Others[37,40,41] have also found that the sulfonamides or streptomycin are of value in treating *Pseudomonas aeruginosa* infections due to sensitive strains. If other forms of antibacterial therapy fail, the use of oral polymyxin B is recommended[36].

Summary

Results obtained in the routine examination of stool specimens of over 5,000 patients at Michael Reese Hospital during 1950 are presented. It was found that certain strains of paracolon bacilli, *Shigella alkalescens* and *Pseudomonas aeruginosa*, especially when present in predominate numbers in the stool culture, were associated with various gastrointestinal infections. Although no conclusive proof was obtained that *Proteus mirabilis* or *Proteus morganii* are intestinal pathogens, we feel that further studies are warranted. *Proteus* species and *Pseudomonas aeruginosa* were frequently isolated from the stools of individuals who had recently received antibiotic therapy.

Oral sulfonamides and/or oral dihydrostreptomycin were effective in the treatment of most infections confined to the intestinal tract due to sensitive strains of paracolon bacilli, *Shigella alkalescens* and *Pseudomonas aeruginosa*. In the majority of instances there was a correlation between *in vitro* sensitivity tests and clinical response to these species. Other antibiotics which were found effective in *Shigella alkalescens* intestinal infections include chloromycetin, aureomycin, polymyxin B and terramycin. Oral polymyxin B is recommended for *Pseudomonas aeruginosa* infections which fail to respond to the other chemotherapeutic agents. Additional studies are needed to evaluate the broad-spectrum antibiotics in the treatment of paracolon infections.

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Discussion

Dr. William W. Lermann (Pittsburgh, Pa.):—This paper so well covers the subject that I wish to congratulate the authors and hope they will, in the future, continue their excellent work and that others will be stimulated to recognize the importance of this great field in gastroenterology, which might well be called the greatest area of chronic infection as well as the most silent area of infection in the entire human body.

The authors state that they feel that it is significant that the average percentage of paracolon colonies isolated on Endo or SS agar plates from patients with gastrointestinal symptoms was 75 per cent of 85 cases, compared to 23.16 per cent in 120 asymptomatic cases. My question is: Which are the pathogenic bacteria in the intestinal tract? Are not almost all pathogens, under certain conditions potentially capable of producing acute disease if they are chronically residing there during asymptomatic periods, ready to invade and attack whenever the mucous membrane of the intestinal tract is no longer intact?

The defenses of the mucous membrane may be lowered by many possible conditions which are in themselves innocuous. Perhaps inspissated feces or food particles are trapped in a diverticuli; perhaps a polypoid irritation occurs; perhaps a varicose blood vessel bleeds; perhaps a chill from weather exposure occurs. Any of these relatively unimportant conditions may inflame the mucous membrane and so lower its defensive mechanism, so that the chronic, silent, asymptomatic infection then becomes an acute, vociferous, and symptom-producing infection; or, is the organism itself a source of substances directly toxic to the host? Are the bacterial endotoxins and exotoxins highly toxic to the animal that has becomes sensitized to them by infection? Perhaps when the chemist collaborates with the immunologist we shall know the chemical basis of harmful effects of bacterial infection.

Several phases of intestinal infection are of supreme importance in these cases:

1. Where did the infection arise?
2. How was it transmitted?
3. What happened to our normal defenses to permit transmission?
4. What damage has it done to other organs and parts of the body?
5. Is our treatment adequate in overcoming the infection?

1. Where does the infection arise?

In the past thirty years we have carried out a "Search for Foci of Infection" in about 7,000 cases. This consists of cultures from postnasal area, throat, gums, sputum if present, bile obtained by duodenal intubation, stool, urine, prostatic secretion and, in women, uterine cervical smears. Bacteria and pus cells were found in the empty stomach contents of approximately 32.5 per cent of the patients. Of these positive patients, 53 per cent showed a collection of mixed bacteria: Streptococci, Staphylococci, Pneumococci, Micrococci Catarrhalis, and so forth; 40 per cent showed Streptococci alone and 7 per cent showed Staphylococci alone, with about an average of 12 cases per year showing tubercle bacilli, all symptom free and unsuspected of having tuberculosis. All of these patients showed one or more of these same bacteria in all or some cultures of the duodenal tract, "B" bile, stool, urine or prostatic secretion.

2. How was the infection transmitted?

By swallowing, especially during sleep.

3. What happened to our normal defenses to permit this transmission?

A. Our first defense is normal gastric peristalsis which prevents too rapid emptying or too long delayed retention of these bacteria; hypomotility is the greater cause.

B. Abnormal hydrochloric acid content.

18 per cent showed achlorhydria or marked hypoacidity
32 per cent showed hyperacidity
50 per cent showed approximately normal acid content

These various degrees of acidity couped with hypo- or hypermotility permit bacteria to pass into the intestinal tract without being destroyed. A free hydrochloric acid content of 20 to 40 or hydrochloric acid of corresponding strength in dilution of 1:16 will kill hemolytic Streptococci in ten minutes and in higher dilutions up to 1:64 in one hour. Other common pathogenic bacteria such as Colon Bacillus and Streptococci Viridans and Staphylococci show a similar but lesser degree of susceptibility to normal free hydrochloric acid content; however, we must remember that this antiseptic action is not continuous during the 24-hour period, especially during the

early morning hours of sleep, when all our metabolic functions are at their lowest ebb.

C. An intact mucous membrane and an adequate blood supply to same.

D. Normal peristalsis and adequate bile supply, with no stasis in any part of the intestinal tract. Proper diet is always important to avoid the highly putrefactive or highly fermentative stool.

4. What damage has it done to other organs and parts of the body?

A. Liver function may be subnormal (hepatitis and cholecystitis often present).

B. Indicanuria very marked.

C. Skin disturbances such as types of eczema often present.

D. Asthma, infective in type often found. Dr. Louis Clerf, of Jefferson Hospital in Philadelphia, found the same bacterial infection present in sinuses and aspirated lung pus in 82.4 per cent of 200 cases of bronchiectasis.

E. Kidney, liver and joint as well as eye damage frequently seen.

F. Depression-neuroses and often psychoses seen.

5. Is our treatment adequate in overcoming the infection?

This can be evaluated only over a period of several months by repeating cultures, functional tests and the general disappearance of symptoms and previous positive laboratory findings.

Antibiotics, vaccine, diet, control of the gastrointestinal tract in relation to acidity of stomach and motility of the gastrointestinal tract to prevent stasis with irritation to the mucous membrane are all required in treatment of these cases. Naturally, the necessary surgical or medical treatment of the upper respiratory infection is a must. We must remember that the effect of certain antibiotics will depend considerably upon the diet of the patient. A high protein diet requires larger amounts to curtail Escherichia Coli and members of the acrogens group than when large amounts of milk or lactose are taken. Recent research on metabolic changes with the use of antibiotics would suggest the belief that before long the present antibiotics will be of great value in nutritional problems.

We must remember that the stomach is a "drainage trap" collecting swallowed pus and bacteria. If not destroyed, they pass into the intestinal tract, where they live and thrive because of food, body heat and stasis, with resulting absorption of their toxins or by-products, and often bacteria themselves enter the circulation and lymph stream to be carried to distant parts of the body to produce infective inflammatory processes. Sixty-five per cent of fresh feces is fluid or moisture, but 50 per cent of dried feces consists of dead bacteria.

I have a few slides.

These simply illustrate one thing, that the same organism is so frequently found in various parts of the body. This stool shows hemolytic Staphylococci. If you will notice, the same thing is found in the postnasal region, in the throat specimen, in the urine specimen, and in the prostatic specimen.

The stool in the next slide shows a few Staphylococci. You will find them in the postnasal area, and in the duodenal specimen also.

The next stool shows green and indifferent Streptococci also in the throat, in the duodenal specimen, in the gastric content, and in the urine.

This one shows Streptococci and Staphylococci in the stool, and you will find them in the postnasal culture and the throat culture.

In this slide the stool shows green Streptococci predominating, and you will find them in the throat culture and sputum.

The stool in the next shows Staphlylococci which were found also in the sputum and the postnasal culture and in the throat.

This stool particularly shows the hemolytic Staphylococci which were found in the postnasal cultures and throat cultures.

The last stool culture particularly shows a hemolytic Staphylococcus Albus again found in the postnasal region, throat culture, urine culture, and in the bile.

Dr. Albert Milzer (Chicago, Ill.):—I was very much interested in Dr. Lermann's remarks. I think we must certainly keep an open mind on all aspects of this subject. It should be re-emphasized that we should encourage the laboratory to report the complete bacteriological findings of stool examinations and not just indicate "negative" or "normal". It is the function of the physician to interpret laboratory results in the light of clinical findings. Perhaps in this way the physician can begin to make clinical correlations of the pathogenicity and successful therapy of the borderline intestinal pathogens.

GALLBLADDER DISEASE*†

BRUCE C. LOCKWOOD, M.D.

Detroit, Mich.

Modern improved methods of study, and a knowledge of clinical and animal research, have given us a clearer view of the normal and abnormal physiology of the gallbladder and its relation to the development of organic pathology[1-4,6].

Our concept of gallbladder disease should now postulate that functional disturbances producing stasis precede and cause the organic changes, inflammation, infection and stones, in the great majority of cases[1,5,12,21]. Most teachers and authors have, however, not kept abreast of known facts, and are presenting an obsolete and confused picture of the subject, based upon findings in a late stage of the disease.

A review of normal gallbladder physiology is essential for proper understanding. The gallbladder mechanism converts the continuous secretion of the liver into an intermittent discharge into the duodenum. The secretory pressure of the liver bile is about 300 mm. bile. The sphincter of Oddi, between meals, remains in tonic contraction tightly closed and able to withstand a pressure of 600 mm. bile without letting fluid pass; however, when the pressure in the common duct exceeds 75 mm. bile the valves of Heister yield and bile flows into the gallbladder. In the gallbladder, water is absorbed and the bile is concentrated to 10 to 20 per cent of its original volume. The gallbladder secretes about 25 c.c. mucus daily. It also has definite motor activity, the most common type of which is atonic contraction lasting 10 to 20 minutes, with an expulsive power of about 300 mm. bile[8,9].

The gallbladder empties by an interplay of three mechanisms. Cholecystokinin, a hormone which is liberated in the duodenum by chyme which contains fat, fatty acids or HCl and when absorbed causes the gallbladder to contract. The law of contrary enervation (Meltzer-Lyon) whereby there is a relaxation of the sphincter of Oddi when the gallbladder contracts. A nervous control through the autonomics, in which the tone and rhythm and irritability depends on ganglia in the viscera, but may be influenced by outside stimuli such as emotions, reflexes and toxemias. Stimulation of the vagus by choline or pilocarpine causes contraction of the gallbladder and relaxation of the sphincter of Oddi, while stimulation of the sympathetics by adrenalin causes relaxation of the gallbladder and contraction of the sphincter of Oddi.

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†From the Division of Internal Medicine, Harper Hospital, Detroit.

Any disorder of the filling and emptying mechanism of the gallbladder is termed biliary dyskinesia, of which there are several types.

The mechanism of biliary dyskinesia is similar to that of constipation; in fact, the two conditions occur together so often as to indicate a common etiology[10]. Constipation may be of the atonic type with absence or diminution of peristaltic waves, and absence of pain, or it can be of the spastic type, with the occurrence of local spastic areas and colicky pains[11]. Likewise, biliary dyskinesia can be of the hypotonic or of the hypertonic type. In the hypotonic type pains are not present unless inflammation or stones have supervened. In the hypertonic type pains may be present without organic pathology and at times such pains may be severe enough to simulate the pain due to stones. There is a misunderstanding among most clinicians in that their concept of biliary dyskinesia seems to include only the severe spastic painful hypertonic types of the disorder, and not the other less dramatic and less acute hypotonic dysfunctions.

A survey of patients shows that biliary stasis caused by some type of biliary dyskinesia is the major primary etiologic factor in about 80 per cent of gallbladder disease. Stones and cholecystitis occur late in the disorder. This concept has been emphasized especially by Carter, Green and Twiss[12].

The types of early gallbladder disorders are as follows:—

1. *Hypotonic Biliary Dyskinesia:*—In this type of functional motor disorder of the biliary tract, the gallbladder does not adequately contract and empty. This may be due to an absence or diminution of the normal stimuli which causes such contraction, or to a constitutional low reflex activity.

The typical patient type with this condition is described by the old statement "Fat, fair and forty and belches gas". Modern parlance has given the description with seven F's. Female, Fat, Fair, Forty, Flatulant, Flabby and Fertile. These patients usually give a history of eating little or nothing at the morning and noon meals and an average meal at night. Careful questioning and honest answers, however, reveal that many calories are taken as carbohydrate pastry snacks throughout the day. Thus a stimulus to gallbladder contraction has been given only once per day for probably many years, hence gallbladder stasis and the development of stones, and often inflammation.

The symptoms are usually mild epigastric distress, bloating and belching coming soon after eating. Atonic constipation with the cathartic habit is common. This type of dyskinesia initiates about 40 per cent of all gallbladder disease cases.

X-ray examination shows a large pear-shaped gallbladder with moderately good filling and concentration of the dye but rather sluggish after fat contraction. Later there develops one or several large cholesterol stones. It is a lazy atonic gallbladder, and when inspected after removal, the wall is thin, unless as often occurs late in the disease, there has supervened a chronic fibroid cholecystitis.

Duodenal drainage usually gives a poor response of dark bile after magnesium sulfate instillation, it is augmented after olive oil; cholesterol crystals are usually found in the dark bile.

Gastric analysis usually shows low or absent hydrochloric acid.

The basal metabolism rate is often below normal, and the blood cholesterol above normal.

Treatment of Hypotonic Dyskinesia:—The condition responds well to medical management. If the patient is obese a 1,200 calorie balanced diet is advisable until the ideal weight has been attained, then a normal balanced diet. Three balanced meals should be taken daily, each containing a tablespoonful of olive oil and also one or two cubes of vegetable butter substitute in order to promote evacuation of the gallbladder three times daily. Foods, high in cholesterol, such as fats of animal origin, butter, cream, egg yolk and fat meat, and also brain, kidney, pancreas and salmon should not be eaten. If the stomach acid is low or absent dilute hydrochloric acid should be taken with each meal in order to promote the formation of cholecystokinin and gallbladder evacuation. If the basal metabolism is low the administration of thyroid extract is indicated. Constipation should be corrected by diet, supplementary Vitamin B foods, such as wheat germ or powdered yeast, and often by the administration of hydrophilic vegetable bulk producers.

Bile stasis is eventually followed by cholesterol precipitation and stone formation if not properly treated. When stones have formed the symptoms usually remain the same unless a stone becomes impacted in the neck of the gallbladder, then attacks of severe colicky pain may occur. Once the stone has become permanently stuck in the gallbladder ampulla, the colicky pains may diminish because the gallbladder wall tends to become atonic. Discomfort in the right upper abdomen may then become more constant but with exacerbations after fatty meals which stimulate the gallbladder contractions. Soon the gallbladder becomes distended and inflamed. The gallbladder then may fail to visualize by x-ray examination. When stones have formed, surgery is indicated to prevent such progressive complications. If surgery is not done, the gallbladder may later become thickened fibrotic and contracted, with superimposed infection which may extend to the common duct and to the liver.

2. Hypertonic Biliary Dyskinesia:–The mechanism involved in this type of gallbladder motor dysfunction lies in the sphincter of Oddi at the lower end of the common duct where there is an increase of tone and spasm and often hypertrophy of the muscle fibres. This produces an increased resistance against the contracting force of the gallbladder to the emptying of bile into the duodenum. The result is gallbladder stasis and also a large gallbladder with hypertrophy of the musculature. Pains may be due to sphincter of Oddi spasm or to increased pressure and distention in the common duct or in the contracting gallbladder.

The typical patient with this condition is the nervous, tense, anxious, ambitious person who has difficulty in relaxing and who has never learned the art of continuous inactivity.

The symptoms before complications have ensued may be very mild. They are similar to or associated with gastric hypersecretion, hyperacid gastritis, duodenitis, duodenal ulcer, spastic constipation, the irritable colon and general nervous tension. At times, when the condition becomes acute and intense, there may be severe colicky pains which simulate stone pains. Such acute dyskinesia pains are relieved instantly by the inhalation of amyl nitrite, whereas the pain due to stone usually requires morphine.

X-ray examination shows normal filling and concentration with delayed evacuation. The gallbladder typically is long and tubular rather than pear-shaped. At operation the walls are thickened and hypertrophied. Stones, inflammation and infection appear late in the disease. Regurgitation or pancreatic juice into the gallbladder is found in many cases of cholecystitis when secondary to hypertonic dyskinesia. Such regurgitation is thought to produce a chemical cholecystitis[13,14].

Duodenal drainage usually gives an irregular response to magnesium sulfate and olive oil. Cholesterol crystals may be present if a good dark bile is obtained.

Gastric analysis shows hyperacidity with a prolonged secretory curve, such as seen in ulcer.

Hypertonic dyskinesia is subdivided into several clinical types, namely:

a. Nervous Biliary Dyskinesia:–This is a psychosomatic functional disorder occurring in persons of nervous constitutional type. It is manifested by and associated with gastric hypersecretion, hypertrophic gastritis, gastric and duodenal spasm, duodenitis, ulcer and often papillitis, together with increased nervous tension, anxiety and inability to relax. Environmental emotional factors usually are the precipitating influence.

b. Migraine Biliary Dyskinesia is a subtype of nervous dyskinesia and is quite frequent. It merits special mention because of the therapeutic success obtained with ergotamine tartrate. About 50 per cent of patients with gallbladder trouble have migraine headache attacks.

c. Reflex Biliary Dyskinesia:—A motor dysfunction due to a reflex mechanism from diverticulitis, colitis, pregnancy, pelvic disease, kidney tumors, hernia, etc.

d. Secondary Biliary Dyskinesia, may result from local irritation within the biliary tract itself, such as might be produced by gallstones, inflammatory lesions due to regurgitated pancreatic juice or ingested chemicals or allergy, local injury from rough surgery and duct probing, or from congenital anomalies.

Treatment of Hypertonic Dyskinesia:—Operation on the gallbladder is contraindicated unless there are stones.

A diet should be prescribed which is bland, nonirritating and finely divided, such as is used in ordinary hyperacidity. It should be low in the high cholesterol foods such as animal fat; it should however contain much vegetable, low cholesterol, fat at each meal in order to promote the formation of cholecystokinin and assure a complete emptying of the gallbladder three times daily. The best way to accomplish this is by administration of 15 cc. olive oil before each meal and two cubes margarine with each meal. These fats also promote the formation of enterogastrone which lessens acid secretion. An intake of 2,000 cc. of water daily is important in promoting an abundant thin bile.

Alkalis, such as calcium carbonate, light magnesium oxide or the silicates should be used to neutralize hyperacidity. Sedatives and antispasmodics, especially a combination of belladonna, phenobarbital and the nitrates are of value. Bile salts help in the stimulation of the liver to secrete more thin bile, but they do not promote the emptying of the bile from the gallbladder into the intestine.

A mode of life should be followed which allows and promotes relaxation, avoidance of fatigue, and avoidance of emotional strain.

Psychotherapy should include: Reassurance, which can only be given after complete medical examinations. A friendly attitude. An explanation of the mechanism by which emotional disturbances influence the physiology of the involuntary system, called re-education by the psychiatrist. A sublimation of abnormal psychic tendencies into channels of harmless, useful, entertaining, social or educational use. Environmental changes and advice in connection with type of work, climate, location, marriage or divorce, living within income, or use of contraceptives[15].

Reflex biliary dyskinesia should be excluded by a careful search for and elimination of conditions which might cause such a reflex, especially reflex biliary dyskinesia stasis commonly found in pregnancy[16, 17].

3. *Congenital Anatomical Defects:*–This condition is the etiologic factor in about 5 per cent of gallbladder disease. The biliary tract including the liver arises as a diverticulum from the ventral surface of the foregut just cranial to the yolk-sac. It is, therefore, lined with entoderm and is closely related to the upper abdominal organs as to blood and nerve supply, motor, secretory and absorptive functions. Two solid buds of cells form the two lobes of the liver. The original diverticulum forms the hepatic and common ducts. The gallbladder arises as a solid bud of cells, which later acquires a lumen and the cystic duct by a process called vacuolization. There are developmental defects and variations not infrequently. There is no gallbladder normally in the horse, the deer, the rat and the mouse.

Before the routine use of cholecystography, congenital gallbladder deformities were considered to be rare anatomical curiosities. Recent studies[18] have shown, however, that such anomalies are present in about 3 per cent of cholecystogram examinations and that such defects are prone to cause stasis and disease.

Following are the developmental defects which are most frequently found. Gallbladder deformities such as the folded fundus gallbladder, Phrygian cap, abnormal septa in gallbladder. These comprise the great majority of congenital deformities. They are diagnosed only by careful x-ray examination. Cystic duct convolution. Heister valve obstruction. Abnormal cystic artery crossing and compressing the cystic duct. Congenital cystoduodenal fold and adhesions distorts the cystic duct, producing partial obstruction. Stricture of common duct or ampulla of Vater.

Treatment for these congenital defects is surgical cholecystectomy, providing such anomalies are causing symptoms, or if stones have developed. If the condition is not serious, medical measures which promote gallbladder evacuation three times daily may prevent the development of serious complications.

4. *Primary Gallbladder Infection:*–Primary infection cholecystitis accounts for only about 10 per cent of gallbladder disease. It occurs as a result of some general infection, sepsis, tonsillitis, pneumonia, or some abdominal infection such as appendicitis, diverticulitis, colitis, etc.

Secondary infection, inflammation and stones occur usually after long continued biliary stasis.

The only organisms which can live in bile are the typhoid, colon, Friedlander and Welch bacilli. The streptococcus and staphylococcus are killed by bile, but they may be found in the gallbladder wall and also in the cavity in cases of old cystic duct obstruction and gallbladder empyema[19].

Hepatitis, focal or diffuse, often occurs in cases of any general sepsis, and may be associated with cholecystitis, pancreatitis, appendix and ascending colon. In hepatitis the bile composition may be altered, with concentration and precipitation of mucus, or the precipitation of calcium bilirubinate as small dark irregular pigment granules[20].

Repeated attacks of acute cholecystitis leads to chronic cholecystitis, fibrotic contracted gallbladder, calcium carbonte in wall or lumen, empyema, cholangitis and hepatitis.

Acute cholecystitis may result from and follow some acute general infection such as sepsis, tonsillitis or pneumonia, but more often is an acute exacerbation of a chronic conditon due to previous stasis inflammation, cystic duct obstruction or stones.

Symptoms of acute cholecystitis are severe continuous ache or pain in the right upper abdomen which may radiate to the back under the right scapula which is the spinal segment of the eleventh and twelfth vertebra, or it may radiate in cases of local peritonitis, to the right shoulder due to phrenic nerve irritation and be felt over skin areas supplied by the third and fourth spinal segments which give rise to the phrenic nerve. Septic fever with chills, white cells 10,000 to 20,000. Tenderness and spasm of the right upper abdomen. Enlarged liver indicates cholangitis and hepatitis. An enlarged gallbladder may occur if the cystic duct is obstructed. There may be slight jaundice. X-ray dye examination shows poor gallbladder function.

The treatment of acute cholecystitis is early operation as soon as the diagnosis is made. The operative mortality rate is lowest if done during the first week, if operation is delayed the condition may subside but be recurrent. Medical management consists of complete bed rest, hot applications, a diet of small two-hour feedings with no fat, and the use of penicillin, sulfadiazine or streptomycin as in any other acute severe infection.

Chronic cholesystitis is a common cause of chronic digestive symptoms. Three types of symptoms may be present: Acute severe right upper abdomen pain attacks having no relation to meals, but occurring more likely in the night or after exertion. In this group 75 per cent are found to harbor gallstones. Constant dull pain or soreness in the right upper abdomen. In this group about 25 per cent have been found to have stones. Epigastric bloating and distress or epigas-

tric or substernal burning coming soon after meals, with occasional nausea or vomiting. This is a reflex stomach dysfunction. Stones are found in about 25 per cent of this group.

5. *Metabolic disorders* are the cause of only about 5 per cent of gallbladder disease.

Hypercholesterolemia is found in obesity and in pregnancy, and are prone to develop gallstones. In both conditions however, biliary dyskinesia and stasis are also present, and it is improbable that a high blood or bile cholesterol could influence the formation of gallstones without the presence of gallbladder stasis.

Congenital hemolytic jaundice, is characterized by an increased red blood cell fragility. Calcium bilirubinate gallstones have been found in about 60 per cent of these cases. The treatment is splenectomy.

Splenic anemia and hepatitis cases exhibit high incidence of stones.

Summary and Conclusions

Gallbladder disease is due mainly to a disorder of function which produces biliary stasis. There are five main types of gallbladder disease, each of which may be found in different stages of development and severity. Each may require different treatment. These include: Hypotonic biliary dyskinesia. Hypertonic biliary dyskinesia, with its several sub-types. Congenital anomalies. Primary gallbladder infection. Metabolic diseases.

The development of stones, inflammation and infection constitutes a late stage of the disorders, and are the result of long continued stasis.

This concept of gallbladder disease seems to fit physiologic states as well as the clinical picture actually seen in patients. Medical treatment is of greatest value before the development of stones and inflammation, but should also always be followed in later stages of the diseases before and after operation. When stones have developed or permanent cystic duct obstruction has occurred the gallbladder should generally be removed surgically because of further ensuing complications. At times however, in old people it is perhaps best to leave silent stones alone.

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Discussion

Dr. Samuel Weiss (New York, N. Y.):—Dr. Lockwood has given us a paper on gallbladder disease. I am not going to discuss the entire paper. It would take hours to go over the problem.

I should like to mention two or three items Dr. Lockwood has not mentioned. Allergy of the gallbladder is a very important subject. You will find a great many patients come to your office compaining of pain in the right upper quadrant. These patients have had x-rays and therapy of all kinds without any result. When you question these patients, you will find that they have had hives, or they are subject to hives, or hayfever, or asthma, and if you will take into consideration that the gallbladder and the liver are subject to allergens, you will be able to treat many of these patients medically.

We have seen many patients of this type and one patient particularly, a cook, whose appendix was removed without result. Two or three years later she developed the same symptoms, in the right upper quadrant and was again operated on and this time her gallbladder was removed. She was well on leaving

the hospital. A day or two later, after she returned home, she cooked her favorite dish, green peas, and, lo and behold, developed the same right upper quadrant pain, and this time she developed hives and had to be given a dose of adrenalin which caused the hives to disappear.

The second condition I should like to touch on is that of arthritis. We find that liver and gallbladder conditions becomes a focus, in a great many patients, in fact 70 per cent of the patients may develop arthritis.

In 1932 Drs. Rawls, Collins and I studied this problem at the New York Polyclinic Medical School and Hospital. Out of 100 patients we found over 70 per cent who complained of pains in the joints had some liver and/or gallbladder infection. In 1937 and in 1939 we published the results of our investigation in the *Annals of Internal Medicine*. Since then these findings were verified by clinicians in this country, and in Europe.

There is another condition that may be overlooked in patients having biliary involvement, dyskinesia, without any signs or symptoms of stone, who often have pain in the left chest which resemble anginal attacks. Naturally when they complain of pain in the left chest only, the physician prescribes a tablet of nitroglycerin, to be dissolved under the tongue with almost immediate relief of the pain.

A physician on my staff at one of the hospitals had anginal attacks which were diagnosed as a coronary insufficiency or sclerosis. A day or two after the anginal attack, the EKG showed the first and second leads to be reversed. At times you may find this during or after gallstone attack due to anoxemia of the myocardium. Ten days after she was hospitalized, she had a severe attack of right upper quadrant pain, and in spite of the diagnosis of the cardiologist, I insisted on x-ray examination with the dye which revealed a large stone in the gallbladder. After the gallbladder attack subsided she was operated on and since then hasn't had any coronary or anginal attacks.

Dr. Katz, has had several patients who did not manifest any symptoms of gallbladder condition but all had pain in the left chest, and they were operated for stones in the gallbladder, and since then these patients have not had attacks.

A ROENTGENOGRAPHIC EVALUATION OF THE COMMON MEASURES EMPLOYED IN THE TREATMENT OF COLONIC STASIS*†

HARRY BAROWSKY, M.D.

New York, N. Y.

Many procedures are employed today to induce bowel evacuation. The object of this investigation was to evaluate the efficacy of the more common practices. The treatment of functional constipation may be divided into general and specific therapeutic measures. Where organic lesions are responsible for the colonic stasis, it is self-evident that eradication of the underlying pathology is necessary.

The aim of the general therapeutic measures is essentially corrective. Their object is to produce an optimum condition for reestablishing normal bowel func-

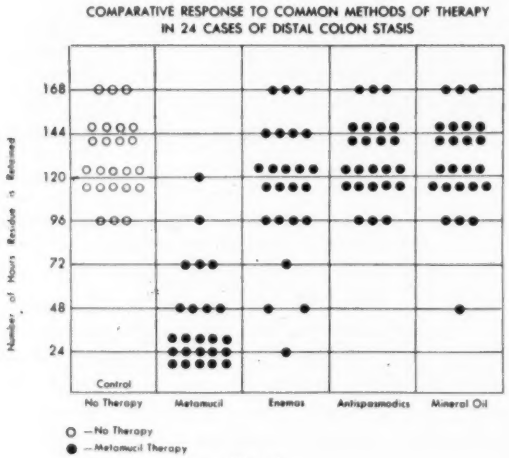

Fig. 1

tion. These procedures consist of cessation of the use of cathartics, the establishment of a proper dietary regime providing for adequate intake of roughage, fluid and vitamins, the regulation of bowel habit; moderate exercise; elimination of mental stress and the adjustment of endocrine dysfunction. The above measures are well-known and will not be amplified in this communication. In this

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†From the Department of Medicine, Section Gastroenterology, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y. This study was aided by a grant from G. D. Searle & Co.

investigation, the patient was given an adequate trial of these methods. All those that failed to respond were selected for a more specific type of treatment. The specific measures employed in this investigation are those which are commonly used to induce bowel evacuation. Our aim was to rid the patient of the undesirable laxative habit and to substitute a mild evacuant. The procedures evaluated were a hydrophilic mucilloid substance, enemata, mineral oil, antispasmodics and sedatives and finally cathartics were tried if the above measures failed.

A discussion of the treatment of colonic stasis will necessarily depend to a large degree on our understanding of the dysfunction of the colon occurring in this type of disturbance. Clinical precepts reflect a lack of knowledge of this problem because the physiologic concepts are incomplete.

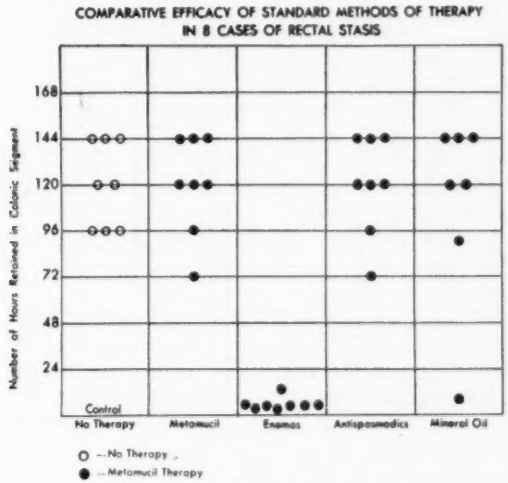

Fig. 2

Functional constipation is essentially a derangement of the propulsive mechanism of the colon, whereas absorption of fluid and secretion of mucus play a relatively minor role. A more informative study must necessarily be based on motility. A roentgenographic method[1] of evaluating the segmental emptying time of the colon gave us the best objective understanding of the problem.

The patient was given a mixture of barium sulfate orally. Fluoroscopic observations were then made at twenty-four or forty-eight hour intervals until no more contrast medium was seen in the gastrointestinal tract. The emptying time of the segments of the colon as well as the total emptying was recorded. Three relatively independent basic patterns of abnormal colonic retention were

observed. They were classified as proximal colon stasis, distal colon stasis and rectal colon stasis. Occasionally combinations of these types occurred and a pseudostasis, chiefly observed in the neurotic patient, also was identified. Once we had objective evidence that we were confronted with different types of constipation, then as a logical sequence the most effective treatment for each type had to be ascertained. To accomplish that it was essential to evaluate the most common procedures employed to induce evacuation, in each type of colon stasis.

Method of Study

After determining the type of stasis the patient had by fluoroscopic observation, he was given a few days rest and the second phase of the investigation was instituted.

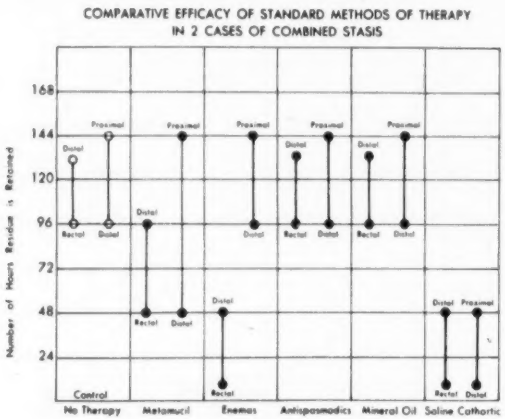

Fig. 3

This consisted of evaluating his response to therapy. At the start, a mucilloid substance (Metamucil) derived from plantago ovata was selected. It was administered by mixing three teaspoonfuls of the product with the regular barium contrast medium. The patient was then instructed to take the mucilloid for several weeks at the start, a dram, two to three times a day in a glass of water and stay on a normal diet. Fluoroscopic observations were again made as in the previous study[1] and the emptying times of the colonic segments were again recorded so that a comparison of the colonic segmental emptying time with and without therapy could be made. In a similar fashion, the patients were then investigated by exposing them to enemata, mineral oil, antispasmodics and sedatives and finally, saline cathartics if the above measures failed.

A total of fifty cases were studied. Since fifteen of our patients were of the pseudostasis variety and they had no problem of delayed emptying, they will be discussed separately.

The response to the mucilloid therapy was uniformly good in twenty-four of the remaining thirty-five patients. All the twenty-four cases were of the distal colon stasis variety. The distal colon emptying time was reduced from an abnormal 96 - 168 hours to 24 - 48 hours (Fig. 1). The bulk producer apparently initiated the "mass movements" which were relatively infrequent in these individuals. Unusually good results with mucilloid substances have been reported by others[2,3]. On the other hand, the remaining eleven patients having rectal and proximal colon stasis showed no response, whereas the two combined stasis responded partially (Fig. 3).

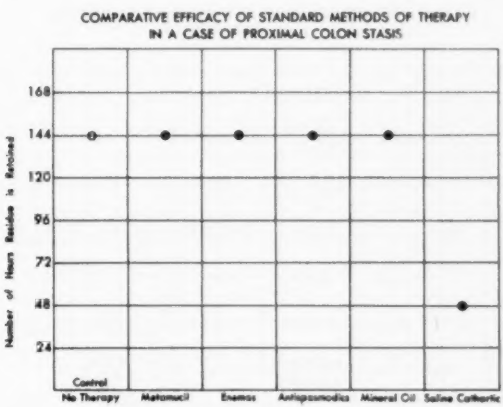

Fig. 4

The dose of the mucilloid used varied from one dram in a glass of water, twice daily, to two drams, three times a day. No immediate results were obtained. In some instances, the effects were observed in twenty-four hours. However, in the majority of cases, it took forty-eight and, in a few, seventy-two and ninety-six hours before the initial bowel evacuation took place. After that, if the patient continued to take the product, elimination became regular. However, when treatment was interrupted and the patient was given a rest period, the original disturbance of constipation usually returned.

Mineral oil was then prescribed to the same group. Three out of the thirty-five cases showed an improved emptying time, two were moderate cases of rectal stasis (Fig. 2) and one was a distal colon stasis (Fig. 1). In the remaining thirty-two no improvement was observed. Most of these individuals complained of

the discomfort of having the oil come through without inducing any evacuation. In addition to being ineffectual in most instances, many harmful effects have been attributed to mineral oil[3,4,5,6,7,8].

Rectal enemata were then administered to the same thirty-five cases. This type of therapy proved completely effective in only eight cases, all being of the rectal stasis variety (Fig. 2). The empyting time of the rectum was reduced from an abnormal 72 - 144 hours to 0 - 24 hours. Eight to sixteen ounces of plain lukewarm water was given every morning for the first week. The second week the enemata were taken every other morning. The frequency of the enemata was then decreased according to the progress the patient was making. Usually by the fourth week only two enemata weekly were needed and in most instances none at all by the sixth to eighth week. Oil retention enemata may be substituted,

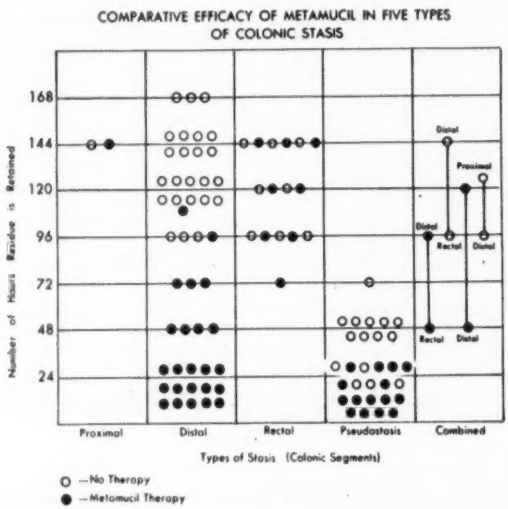

Fig. 5

as they were equally efficacious. Glycerin suppositories proved effective in a few cases. Enemata were partially successful in five of the distal colon stasis patients and had no effect on the remaining twenty-two.

Spasm of descending and sigmoid colon was treated as a possible cause for colonic retention in all thirty-five patients. The therapy consisted of the administration of graduated doses of the Tr. of Belladonna, starting with 10 minims and increasing it a drop at a time until the patient complained of a dryness or flushing. In addition some sedation was also given in the form of phenobarbital ¼ grain. No significant response was observed in any of our patients (Figs. 1-4).

It is possible that some of these individuals may respond to psychotherapy in accord with the principles suggested by Almy[9].

Three cases consisted of two combined (Fig. 3) and one proximal colon stasis (Fig. 4). One of the combined stasis was of the distal rectal variety. This individual had to resort to enemata and in addition, at times also take the mucilloid in order to obtain effective results. Another case was a proximal distal type of retention. Repeated enemata in this patient were ineffectual. The mucilloid product caused normal emptying of the distal colon, but did not affect the proximal colon (Fig. 3). The only way this individual could obtain complete evacuation was by the use of saline cathartics. Small doses of $MgSO_4$ twice daily were effective. The last case had proximal colon stasis (Fig. 4). None of the standard methods of treatment was of any avail except saline catharsis. This was the only effective measure that reduced the proximal colon emptying time from 144 hours to 48 - 72 hours.

The problem of the individuals with pseudostasis was not that of delayed colonic emptying, but it resolved itself rather in the alleviation of their neurotic symptoms. Reassurance of this type of individual that they had normal bowel function and that slight variations in bowel habit were normal seemed to have no effect. Explaining to them the normal x-ray findings also was not convincing. In most cases the patient insisted on having "a good bowel movement". In such instances, small doses of Metamucil were prescribed. The results were excellent. There seemed to be nothing more gratifying to this type of individual than to be able to report that his "tight" headaches, tension and misery seemed to vanish after each "full" evacuation. To them, the miracle of the bowels was a very important attainment in their constant quest for that elusive sense of well being.

Conclusion

Classification of colonic stasis based on roentgenographic observations of the emptying time of colonic segments gives us a better understanding of the altered propulsive mechanism of the colon. With this added knowledge we are in a better position to exploit the treatment of this affliction. A roentgenographic evaluation of the common methods of therapy revealed some interesting findings. It was demonstrated that the least irritating, a mucilloid substance (Metamucil) has been most effective in the most prevalent distal colon stasis, and in pseudostasis (Fig. 5). Enemata gave good results in rectal stasis only. Mineral oil had very little effect. Antispasmodics and sedatives had no efficacy at all. Finally, it was found that the use of habit-forming cathartics may be avoided in most instances. It had to be resorted to in only 2 per cent of our series and that was in the least common proximal and combined colon stasis. A better understanding of this disturbance will obviate many therapeutic errors. For instance, it is foolish to administer cathartics and needlessly irritate the entire

gastrointestinal tract, when only local therapy is necessary to treat rectal stasis. It is equally illogical to persist in the use of ineffectual enemata in proximal and in the majority of distal colon stasis cases. Further studies of this type may evolve a better approach to the treatment of a much neglected affliction.

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EDITORIAL

Physiology of the Biliary Tract

We know that bile normally contains mucoprotein, ammonia, urea, purine derivatives and amino acids. Leucine and tyrosine appear in the bile in cases of severe necrosis. Small amounts of glucose (less than 70 mg. per 100 c.c.) are also present in the fasting state, increasing after the ingestion of foods and in abnormal hyperglycemic states. The usual absence of glucose from gallbladder bile is attributed to rapid glycolysis in that viscus. Only traces of amylase and no lipolytic or proteolytic enzymes are generally present. The only enzyme of significance present in abundance in hepatic bile is phosphatase. Bile also constitutes an excretory medium for many substances, including lead, copper, bismuth, arsenic, mercury, iron, iodine, sulfonamides, salicylates, etc.

In addition to the above, it has been found that bile also excretes large amounts of estrogens, Vitamin D, and other steroid compounds.

Bile pigment in the form of bilirubin and biliverdin are the most important pigments of normal human bile. The pigment of freshly secreted human bile consists practically entirely of bilirubin. Concentration of this pigment varies from time to time (2.3 to 18 mg. per 100 c.c.). In biliary obstruction there is a diminution in the amount of pigment in the bile, this change being masked at times by the concentrating action of the gallbladder. When obstruction of relatively brief duration is present there is a rapid increase in both concentration and total output of bile pigment during the greater part of the first week of decompression, with a subsequent decrease to approximately normal levels. When obstruction has been present long enough to produce permanent hepatic damage, or in the presence of hepatic dysfunction due to other cause, there is a decrease in both the concentration and the total output of bile pigment, frequently with the excretion of relatively large amounts of pale fluid with a low total solid concentration.

As a result of a portion of a damaged extrahepatic biliary conducting system becoming obstructed, the static bile is gradually diluted by the mucoid secretion of the duct epithelium and eventually becomes colorless—white bile. When found in the common bile duct and gallbladder, this white bile is of great prognostic importance, because it contains chlorides and as a rule, calcium similar to that found in the blood serum levels. Cholestrol concentration is low and bile acids are absent; bile pigment is present in extremely small amounts or entirely absent. The theory for the formation of this pathological fluid is that it can be formed only if the hepatic parenchyma is no longer functioning normally.

Decreased solubility of cholesterol in the bile may be due to stasis in the gallbladder, the pH of the bile is lowered and the faculty of bile acids for com-

plete formation is diminished, with a diminution also in their dissolving power. Resorption of water by the gallbladder mucosa raises the concentration of all constituents of the bile, which brings most of the bile components to the limit of their saturation and leads to precipitation. Bile acids may be reabsorbed through an inflamed gallbladder mucosa so rapidly that the bile acid-cholesterol ratio falls to the point where cholesterol is precipitated. The disturbance in this ratio may be aggravated and the inflamed gallbladder mucosa may add relatively large quantities of cholesterol to the contained bile and thus form gallstones.

S. W.

BOOK REVIEWS

CLINICAL RADIATION THERAPY: Edited by Ernst A. Pohle, M.D., Ph.D., F.A.C.R. Professor of Radiology and Chairman, Department of Radiology and Physical Therapy in the University of Wisconsin, Madison, Wisconsin. New (2nd) Edition. 902 pages. 314 illustrations on 201 figures and 16 diagrams. 1 plate in color. Lea & Febiger, Philadelphia, Pa., 1950, Price $15.00.

Among the contributors to this volume are well-known clinicians and each department is written by a specialist in his chosen field.

There are fourteen chapters and two supplements. Chapter one covers Hematology; Leukemia; Chloroma; Lymphogranulomatosis (Hodgkins' Disease); Lymphosarcoma; Leukosarcoma; Lymphoma; Diseases of the Spleen, etc. Chapter two deals with Radiation Therapy of the Circulatory System. Chapter three covers Radiation Therapy of the Respiratory System and the Breast. The other chapters cover Radiation Therapy in gastrointestinal Diseases; Female Genital Organs; Genitourinary Tract; Nervous System; Eye and Ear; Muscles, Bones, Joints and Tendons; Glands of Internal Secretion; Inflammatory Diseases; Diseases of the Skin; Radiation Reactions and Injuries; Liability of the Radiologist. In the two supplements the reader will find discussion of low intensity needles and dosage calculation in radium therapy.

This volume is interesting and instructive not only to the radiotherapist but also to physicians in general. It gives a clear and comprehensive description of diagnosis and differential diagnosis of conditions encountered in daily practice.

THORACIC SURGERY: Richard H. Sweet, M.D., Associate Clinical Professor Surgery, Harvard University Medical School, Illustrations by: Jorge Rodriguez Arroyo, M.D., Assistant in Surgical Therapeutics, University of Mexico Medical School. 345 pages with 155 illustrations. W. B. Saunders Company, Philadelphia, Pa., 1950, Price $10.00.

The illustrations in Dr. Sweet's book on Thoracic Surgery were done by Dr. Jorge Rodriguez Arroyo of the University of Mexico Medical School and are clear-cut and add a great deal to the well printed volume.

Although this volume is of greater interest to the surgeon, especially the thoracic surgeon, the reviewer recommends it highly to the internist. It will give him a general idea of what the well trained thoracic surgeon can do in a given case.

The author and the publisher deserve commendation in the preparation of this excellent volume.

THE EXTERNAL SECRETION OF THE PANCREAS: J. Earl Thomas, M.D., 149 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1950, Price $3.50.

This little volume is written by an eminent physiologist and is one of the "American Lecture Series". It deals with the morphology; experimental methods; pancreatic juice; functions of external secretion; stimuli for the pancreas; secretion and pancreogymin; functional innervation and mechanism of pancreatic secretion.

The text is clear and easily read, the illustrations are explanatory and each chapter is followed by more adequate references. A name and cross-index complete the book.

Laboratory workers and physiologists will find a handy reference in this little volume.

PEPTIC ULCER: A. C. Ivy, Ph.D., M.D., D.Sc., LL.D., Vice President of the University of Illinois in Charge of Chicago Professional Colleges; M. I. Grossman, Ph.D., M.D., Associate Professor of Physiology, University of Illinois, College of Medicine; and William H. Bachrach, Ph.D., M.D., Research Associate in Physiology, University of Southern California, School of Medicine. 137 illustrations; 210 tables; 1,144 pages; The Blakiston Company, Philadelphia, Pa., 1950, Price $14.00.

The foreword to this extensive monograph on ulcer is written by well known authorities, Lana M. Jordan, Donald C. Balfour and A. J. Carlson and is divided into four parts: Introduction to the problem of peptic ulcer; on the pathogenesis of peptic ulcer; diagnostic problems, and a most enlightening chapter on the treatment of peptic ulcer.

Since the appearance of this book, the

reviewer has been reading it with a great deal of pleasure and acknowledges that he has gained information which up to the present time was more or less based on various theories and facts. However, after having re-read many of the statements, he now has no doubts about the soundness of the co-authors experimental and clinical findings.

It would take reams of paper to describe the contents, therefore the reviewer recommends that every physician who is interested in the welfare of his patients, especially patients who have ulcers, should buy and carefully peruse the contents of this highly scientific and clear cut description of the American disease—ulcer.

FROM A DOCTOR'S HEART: Eugene F. Snyder, M.D., with a foreword by Dudley White, M.D., illustrated, 251 pages. Philosophical Library Inc., 1951, Price $3.75.

This book should be read by doctors as well as laymen. The reviewer enjoyed reading the philosophic, religious and medical discussions between the doctor, his wife and son. Both doctor and patient will find a great deal of truth and advice which may save future misery and possible invalidism.

Interesting and instructive reading is the advice of the old physician who lived for more than 25 years after a coronary attack.

Dr. Snyder is to be complimented and the publishers congratulated for bringing this interesting and instructive volume before the public.

HOSPITAL STAFF AND OFFICE MANUAL: T. M. Larkowski, M.D. and A. R. Rosanova, R.Ph., M.D., Chicago, Ill. 428 pages. Illustrated. Romaine Pierson Publishers, Great Neck, N. Y., 1951, Price $5.00.

This little volume is a welcome edition and is highly recommended for senior medical students, interns and the busy physician.

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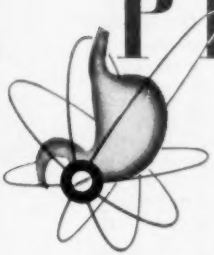

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*Peptic Ulcer. A. C. Ivy, M. I. Grossman and W. H. Bachrach, Blakiston Publishing Co., Phila., 1950.

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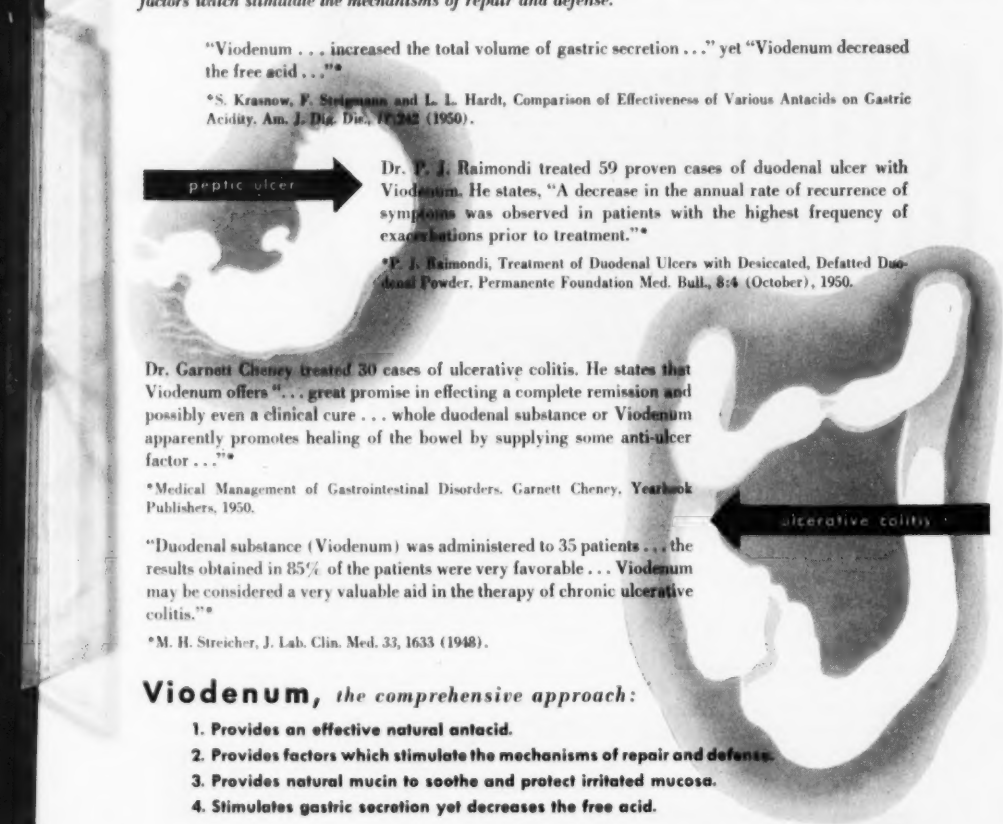
*S. Krasnow, F. Steigmann and L. L. Hardt, Comparison of Effectiveness of Various Antacids on Gastric Acidity. Am. J. Dig. Dis., 17, 242 (1950).



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*P. J. Raimondi, Treatment of Duodenal Ulcers with Desiccated, Defatted Duodenal Powder. Permanente Foundation Med. Bull., 8:4 (October), 1950.

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*Medical Management of Gastrointestinal Disorders. Garnett Cheney, Yearbook Publishers, 1950.

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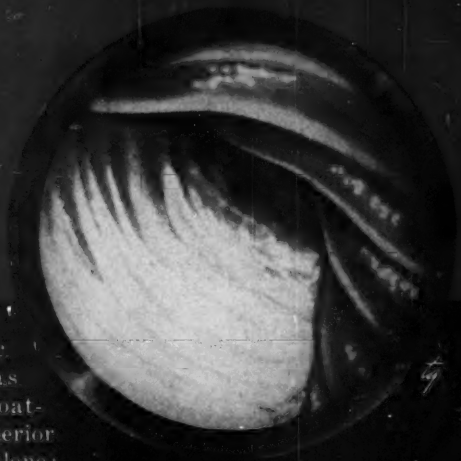

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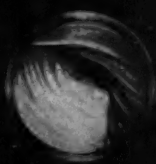

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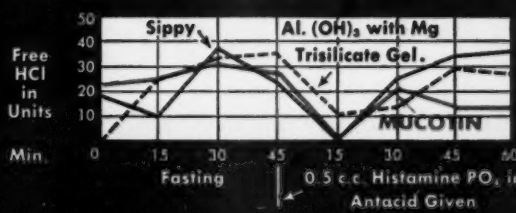

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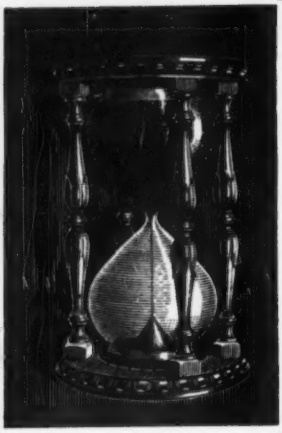

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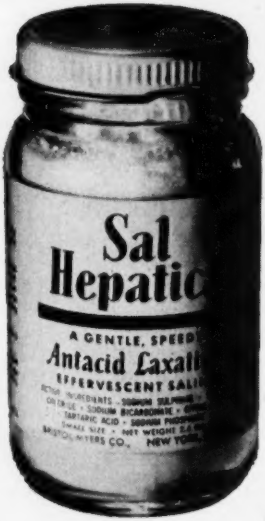

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